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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:35:39 ON 10 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 10 Jun 2005  VOL 142 ISS 25
FILE LAST UPDATED: 9 Jun 2005  (20050609/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L5                STR
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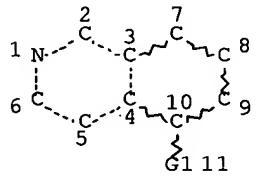


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L7          7759 SEA FILE=REGISTRY SSS FUL L5
L8               STR
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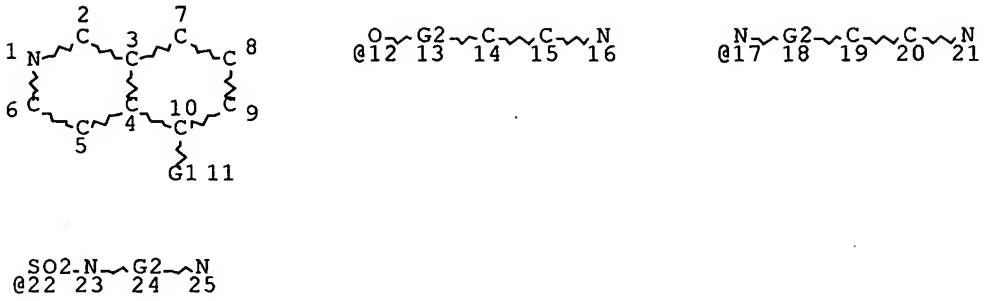

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REP G2=(0-6) C
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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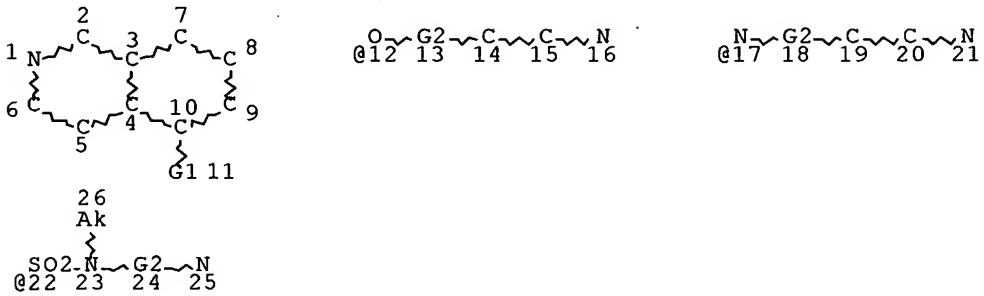
L10 STR



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REP G2=(0-6) C
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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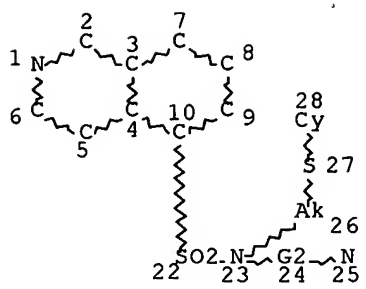

REP G2=(0-6) C
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
L17 28 SEA FILE=REGISTRY SUB=L11 SSS FUL L16
L18 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L17

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=>

=> d ibib abs hitstr l18 1

L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80657 HCAPLUS Full-text
DOCUMENT NUMBER: 140:146016
TITLE: Preparation of 5-substituted isoquinoline derivatives as myosin regulatory light-chain phosphorylation inhibitors
INVENTOR(S): Yamada, Rintaro; Seto, Minoru
PATENT ASSIGNEE(S): Asahi Kasei Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 361 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009555	A1	20040129	WO 2003-JP9158	20030718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2493230	AA	20040129	CA 2003-2493230		20030718
US 2005020623	A1	20050127	US 2003-623751		20030722
PRIORITY APPLN. INFO.:			JP 2002-212053	A	20020722
			JP 2002-327751	A	20021112
			US 2002-397142P	P	20020722
			US 2002-425742P	P	20021113
			WO 2003-JP9158	W	20030718

OTHER SOURCE(S): MARPAT 140:146016

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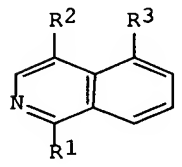

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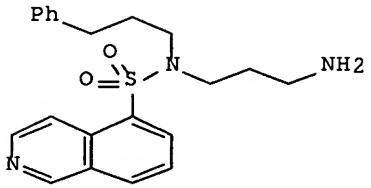


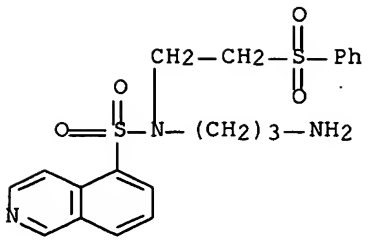
II

AB The title compds. I [wherein R1 = H, halo, OH, NH2, or alkoxy; R2 = H, halo, alkenyl, alkynyl, alkoxy,alkylthio, alkyl-SO, alkylsulfonyl, CN, (un)substituted alkyl, amino, etc.; R3 = (un)substituted OH, SO2NH2, or NH2] or salts thereof are prepared as myosin regulatory light-chain phosphorylation inhibitors. For example, N-(tert-butoxycarbonyl)-1,3- propanediamine was reacted with isoquinoline-5-sulfonyl chloride in CH2Cl2 in the presence of NEt3 to give the sulfonamide. The sulfonamide was reacted with 3-phenyl-1-propanol in THF in the presence of 1,1'-azobis(N,N-dimethylformamide) and Bu3P, followed by hydrolysis to provide II•xHCl. II showed inhibitory activity with IC50 of 0.8 μM against human myosin regulatory light-chain phosphorylation.

IT **651306-92-2P 651306-93-3P 651306-95-5P**
651306-98-8P 651306-99-9P 651307-21-0P
651307-29-8P 651307-39-0P 651307-44-7P
651307-50-5P 651307-55-0P 651309-18-1P
651309-21-6P 651309-25-0P 651309-29-4P
651309-33-0P 651309-37-4P 651309-41-0P
651309-45-4P 651309-49-8P 651309-53-4P
651309-57-8P 651309-61-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of isoquinoline derivs. as myosin regulatory light-chain phosphorylation inhibitors)

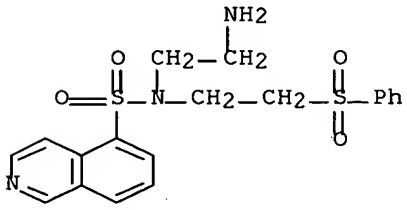
RN 651306-92-2 HCAPLUS

CN 5-Isoquinolinesulfonamide, N-(3-aminopropyl)-N-[2-(phenylsulfonyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 651306-93-3 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(2-aminoethyl)-N-[2-(phenylsulfonyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 651306-95-5 HCAPLUS
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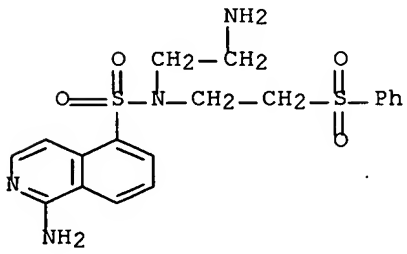
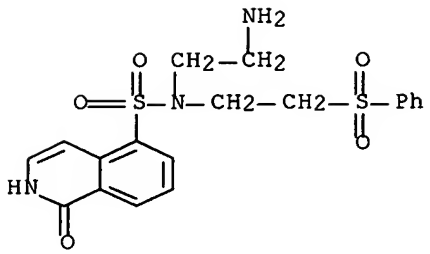


●x HCl

RN 651306-98-8 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(2-aminoethyl)-1,2-dihydro-1-oxo-N-[2-(phenylsulfonyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

RN 651306-99-9 HCAPLUS
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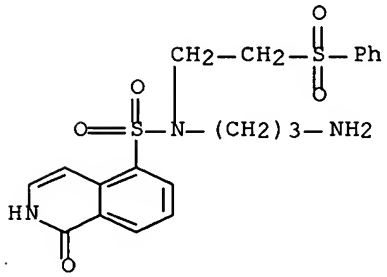

● x HCl

RN 651307-21-0 HCAPLUS
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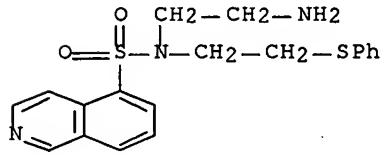
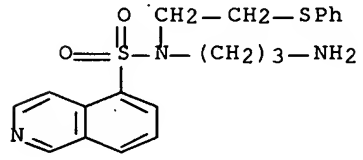


RN 651307-29-8 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(3-aminopropyl)-N-[2-(phenylthio)ethyl]- (9CI) (CA INDEX NAME)



RN 651307-39-0 HCAPLUS
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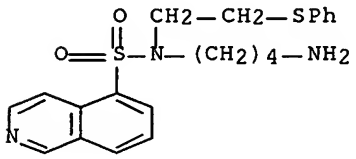
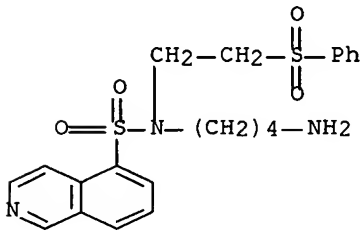


RN 651307-44-7 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(4-aminobutyl)-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



RN 651307-50-5 HCAPLUS
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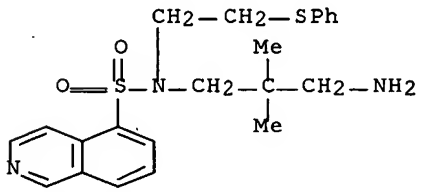

RN 651307-55-0 HCAPLUS
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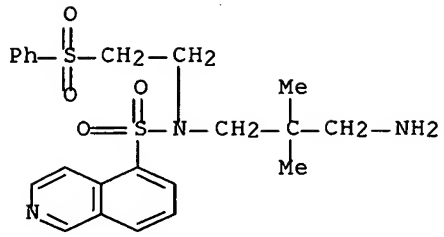

RN 651309-18-1 HCAPLUS
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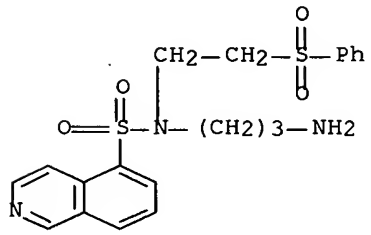
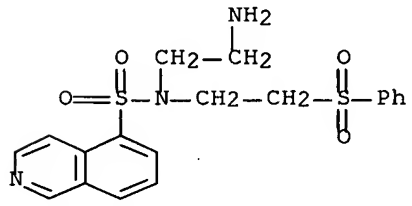


RN 651309-21-6 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(2-aminoethyl)-N-[2-(phenylsulfonyl)ethyl]-(9CI) (CA INDEX NAME)



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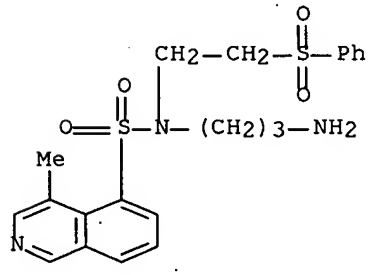
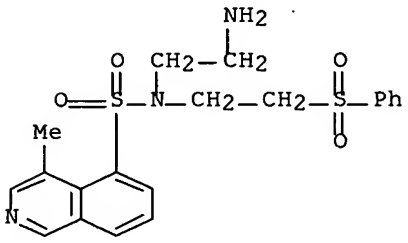
CN 5-Isoquinolinesulfonamide, N-(3-aminopropyl)-4-methyl-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



RN 651309-29-4 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(2-aminoethyl)-4-methyl-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



RN 651309-33-0 HCAPLUS
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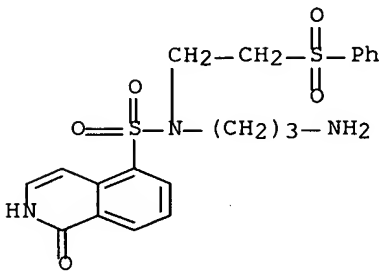

RN 651309-37-4 HCAPLUS
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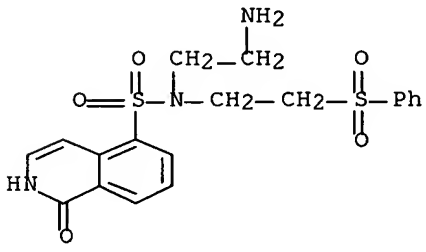
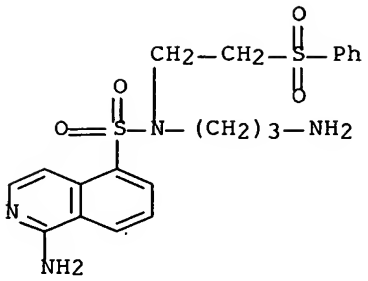
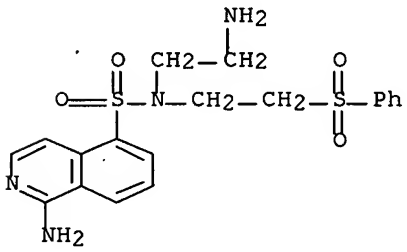


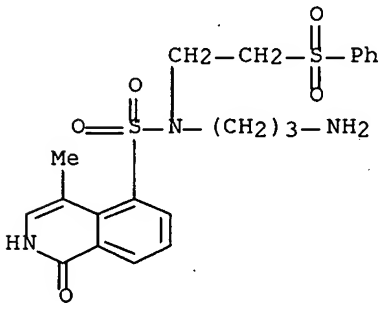
RN 651309-41-0 HCAPLUS
CN 5-Isoquinolinesulfonamide, 1-amino-N-(3-aminopropyl)-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



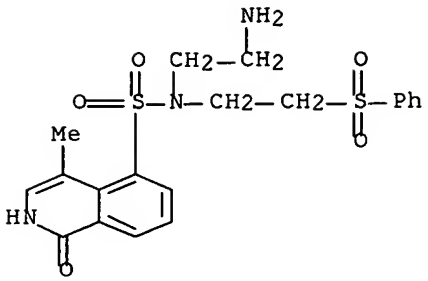
RN 651309-45-4 HCAPLUS
CN 5-Isoquinolinesulfonamide, 1-amino-N-(2-aminoethyl)-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



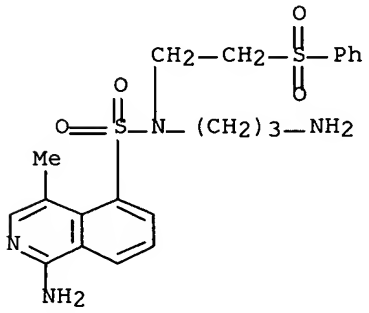
RN 651309-49-8 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(3-aminopropyl)-1,2-dihydro-4-methyl-1-oxo-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



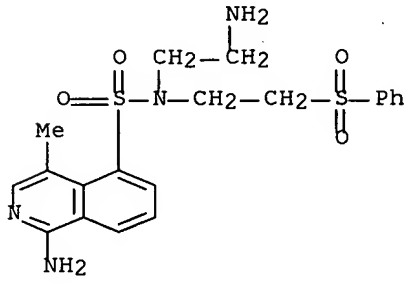
RN 651309-53-4 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-(2-aminoethyl)-1,2-dihydro-4-methyl-1-oxo-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



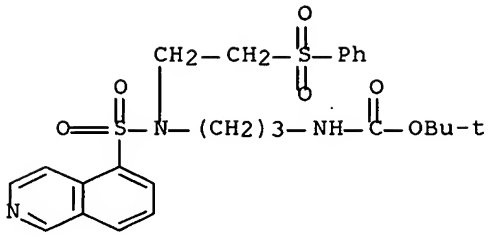
RN 651309-57-8 HCAPLUS
CN 5-Isoquinolinesulfonamide, 1-amino-N-(3-aminopropyl)-4-methyl-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



RN 651309-61-4 HCAPLUS
CN 5-Isoquinolinesulfonamide, 1-amino-N-(2-aminoethyl)-4-methyl-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



IT **651309-71-6P 651309-73-8P 651309-79-4P**
651309-86-3P 651309-87-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of isoquinoline derivs. as myosin regulatory light-chain phosphorylation inhibitors)
RN 651309-71-6 HCAPLUS
CN Carbamic acid, [3-[(5-isoquinolinylsulfonyl)[2-(phenylsulfonyl)ethyl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 651309-73-8 HCAPLUS
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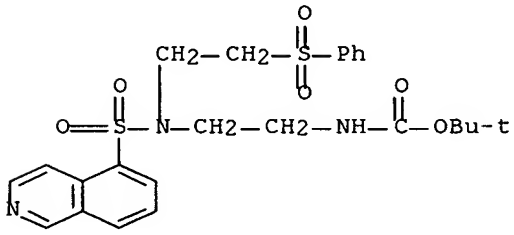
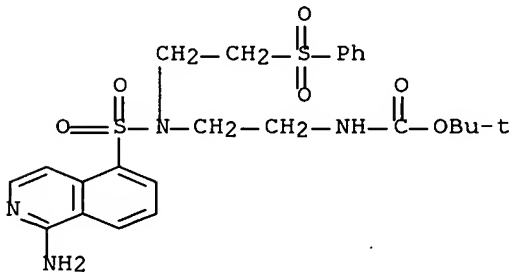
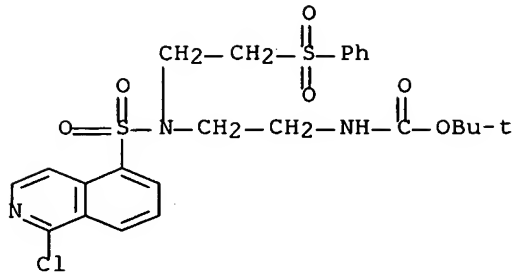


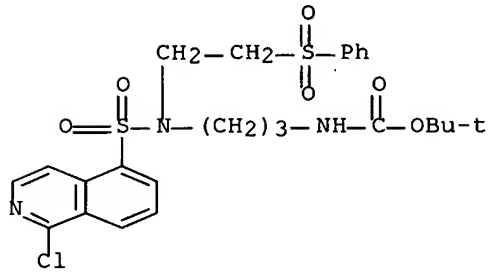
RN 651309-79-4 HCAPLUS
CN Carbamic acid, [2-[[(1-amino-5-isoquinolinyl)sulfonyl][2-(phenylsulfonyl)ethyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 651309-86-3 HCAPLUS
CN Carbamic acid, [2-[[(1-chloro-5-isoquinolinyl)sulfonyl][2-(phenylsulfonyl)ethyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 651309-87-4 HCAPLUS
CN Carbamic acid, [3-[[(1-chloro-5-isoquinolinyl)sulfonyl][2-(phenylsulfonyl)ethyl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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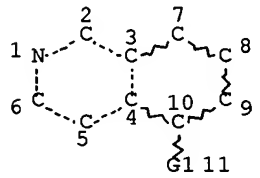

VAR G1=O/N/SO2
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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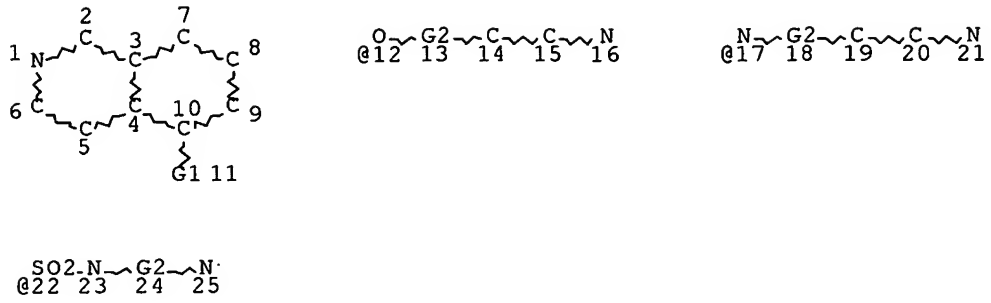
L8 STR



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REP G2=(0-6) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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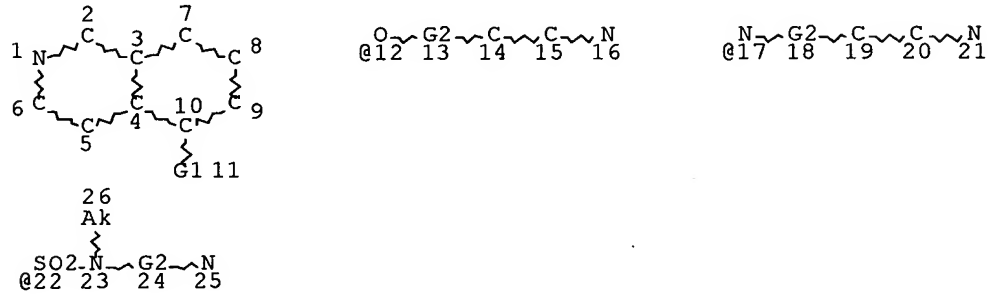

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REP G2=(0-6) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
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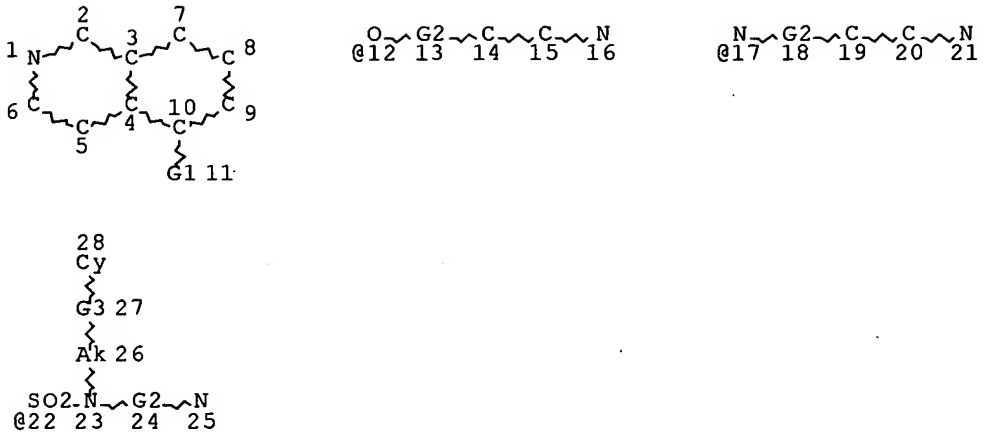
L12 STR



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REP G3=(0-1) S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
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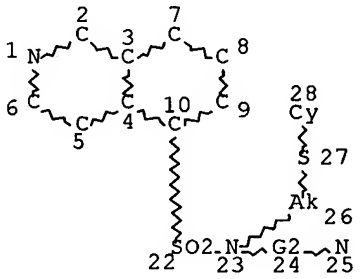
L16 STR



REP G2=(0-6) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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L19 371 SEA FILE=REGISTRY ABB=ON PLU=ON L13 NOT L17
L20 227 SEA FILE=HCAPLUS ABB=ON PLU=ON L19
L21 226 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 NOT L18

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L22         180 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND PD=<NOVEMBER 22, 2002

L25           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND (?MYOSIN? OR LIGHT(2W)
                CHAIN OR ?PHOSPHOR?(5A)INHIBIT?)
L26           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND L25


=>
=> d ibib abs hitstr l26 1-2

L26  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:       2002:521462  HCAPLUS Full-text
DOCUMENT NUMBER:        137:88442
TITLE:                  Incensole and furanogermacrens and compounds in
                        treatment for inhibiting neoplastic lesions and
                        microorganisms
INVENTOR(S):            Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S):     Ire.
SOURCE:                 PCT Int. Appl., 68 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:          Patent
LANGUAGE:               English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ---------------     ----   --------    --------------------     --------
     WO 2002053138        A2    20020711    WO 2002-IE1              20020102 <--
     WO 2002053138        A3    20020919
         W:  AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD,
             UA, UG, US, VN, YU, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI,
             ML, MR, NE, SN, TD, TG
     EP 1351678           A2    20031015    EP 2002-727007           20020102
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2004092583        A1    20040513    US 2004-250535           20040102
PRIORITY APPLN. INFO.:                      IE 2001-2           A    20010102
                                            WO 2002-IE1         W    20020102
OTHER SOURCE(S):        MARPAT 137:88442
AB   The invention discloses the use of incensole and/or furanogermacrens, derivs.
     metabolites and precursors thereof in the treatment of neoplasia, particularly
     resistant neoplasia and immunodysregulatory disorders.  These compds. can be
     administered alone or in combination with conventional chemotherapeutic,
     antiviral, antiparasite agents, radiation and/or surgery.  Incensole and
     furanogermacren and their mixture showed antitumor activity against various
     human carcinomas and melanomas and antimicrobial activity against
     Staphylococcus aureus and Enterococcus faecalis.
IT   147318-81-8, KNI-272
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (pharmaceutical formulation further containing; incensole and
        furanogermacrens and compds. as antitumor and antimicrobial agents)
RN   147318-81-8  HCAPLUS
CN   4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-
     [[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-
     oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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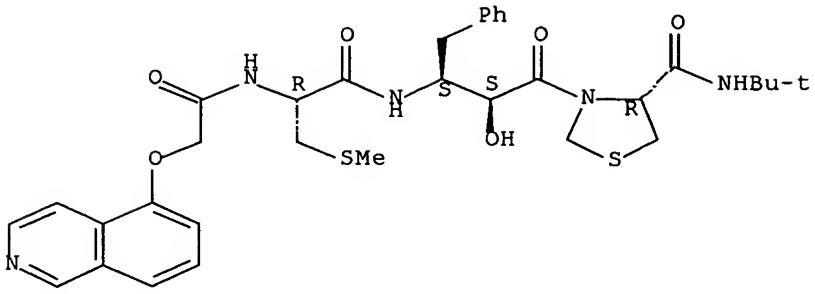

L26 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:185126 HCAPLUS Full-text
DOCUMENT NUMBER: 136:247485
TITLE: Preparation of bicyclic pyrrolyl amides as glycogen **phosphorylase inhibitors**
INVENTOR(S): Bartlett, Julie B.; Freeman, Sue; Kenny, Peter; Morley, Andrew; Whittamore, Paul
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020530	A1	20020314	WO 2001-SE1880	20010831 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2417594	AA	20020314	CA 2001-2417594	20010831 <--
AU 2001082833	A5	20020322	AU 2001-82833	20010831 <--
EP 1317459	A1	20030611	EP 2001-961577	20010831
EP 1317459	B1	20040407		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013606	A	20030624	BR 2001-13606	20010831
JP 2004508376	T2	20040318	JP 2002-525151	20010831
AT 263772	E	20040415	AT 2001-961577	20010831
NZ 524011	A	20040827	NZ 2001-524011	20010831
PT 1317459	T	20040831	PT 2001-961577	20010831
ES 2217183	T3	20041101	ES 2001-1961577	20010831
EE 200300083	A	20041215	EE 2003-83	20010831
ZA 2003001013	A	20040505	ZA 2003-1013	20030205
US 2003232875	A1	20031218	US 2003-344506	20030210
NO 2003001024	A	20030305	NO 2003-1024	20030305
BG 107624	A	20040130	BG 2003-107624	20030310
HK 1055299	A1	20041021	HK 2003-107519	20031016
PRIORITY APPLN. INFO.:			GB 2000-21831 A	20000906

WO 2001-SE1880 W 20010831

OTHER SOURCE(S): MARPAT 136:247485

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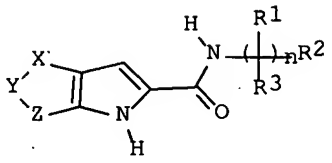

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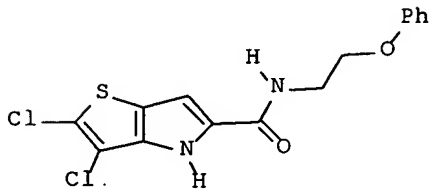


II

AB Title compds. I [R1 = H, halo, NO2, CN , OH, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, NO2, CH2F, CHF2, CF3, amino, alkyl, alkenyl, alkoxy, etc.; R3 = H, alkyl; -X-Y-Z- is selected from -S-CR4=CR5-, -CR4=CR5-S-, -O-CR4=CR5-, -CR4=CR5-O-, -N=CR4-S-, -S-CR4=N-, -NR3-CR4=CR5- and -CR4=CR5-NR3- wherein R4 and R5 = independently H, halo, CN, alkyl, ureido, NO2, etc.; n = 0-4] or a pharmaceutically acceptable salt or an in vivo hydrolyzable ester thereof were prepared possessing glycogen **phosphorylase inhibitory** activity (no data). Thus, II was prepared by amidation of 5-carboxy-2,3-dichloro-4H-thieno[3,2-b]pyrrole with 2-phenoxyethylamine. As glycogen **phosphorylase inhibitors**, I have value in the treatment of disease states associated with increased glycogen phosphorylase activity, e.g., type 2 diabetes. Pharmaceutical compns. containing I are described.

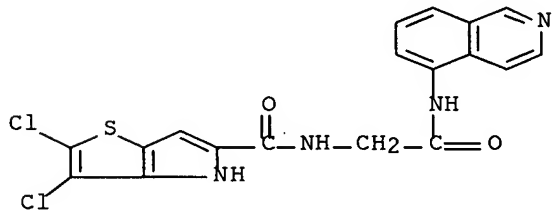
IT **403859-48-3P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of thienopyrrolyl amides as glycogen **phosphorylase inhibitors**)

RN 403859-48-3 HCAPLUS

CN 4H-Thieno[3,2-b]pyrrole-5-carboxamide, 2,3-dichloro-N-[2-(5-isoquinolinylamino)-2-oxoethyl]- (9CI) (CA INDEX NAME)



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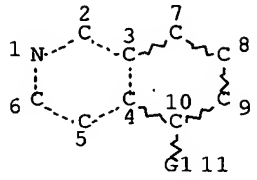

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VAR G1=O/N/SO2
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
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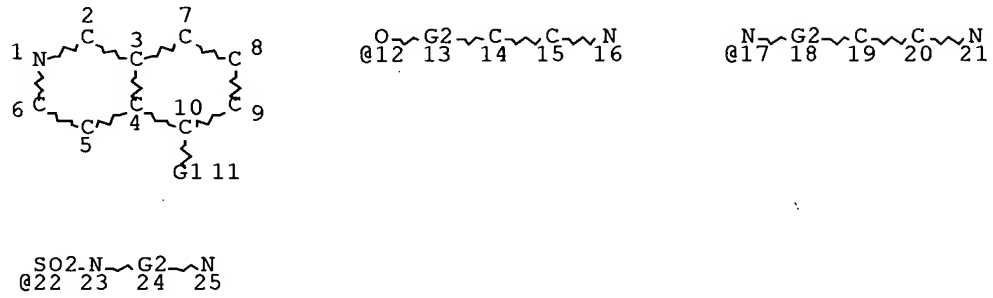

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VAR G1=12/17/22
REP G2=(0-6) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
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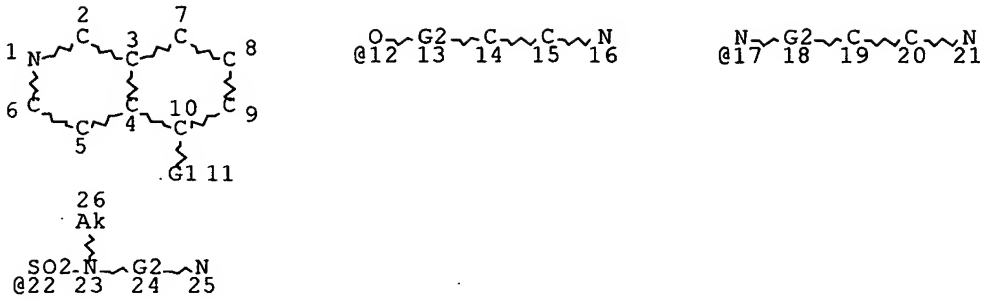

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REP G2=(0-6) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
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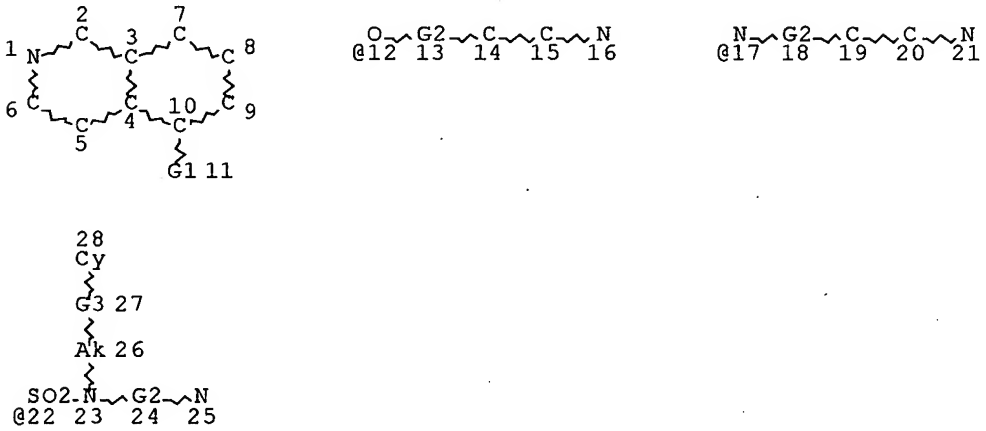
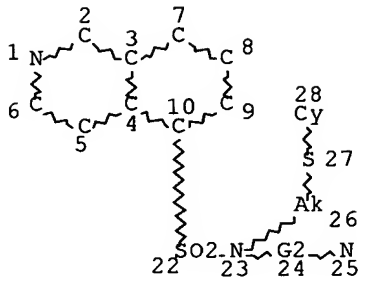
L12 STR



VAR G1=12/17/22
REP G2=(0-6) C
REP G3=(0-1) S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L13 399 SEA FILE=REGISTRY SUB=L9 SSS FUL L12
L16 STR



REP G2=(0-6) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

L17	28	SEA FILE=REGISTRY SUB=L11 SSS FUL L16
L18	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L19	371	SEA FILE=REGISTRY ABB=ON PLU=ON L13 NOT L17
L20	227	SEA FILE=HCAPLUS ABB=ON PLU=ON L19
L21	226	SEA FILE=HCAPLUS ABB=ON PLU=ON L20 NOT L18
L22	180	SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND PD=<NOVEMBER 22, 2002
L23	140	SEA FILE=HCAPLUS ABB=ON PLU=ON L20(L)INHIBIT?
L25	3	SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND (?MYOSIN? OR LIGHT(2W) CHAIN OR ?PHOSPHOR?(5A)INHIBIT?)
L26	2	SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L25
L29	112	SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L23
L30	50	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND PATENT/DT
L31	49	SEA FILE=HCAPLUS ABB=ON PLU=ON L30 NOT (L18 OR L26)

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L31 ANSWER 1 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:793611 HCAPLUS Full-text
DOCUMENT NUMBER: 137:310928
TITLE: Cyanamide, alkoxyamino, and urea derivatives of 4,4-disubstituted-3,4-dihydro-2(1H)-quinazolinones as HIV reverse transcriptase inhibitors
INVENTOR(S): Corbett, Jeffrey W.; Rodgers, James D.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002081456	A1	20021017	WO 2002-US9951	20020327 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003018039	A1	20030123	US 2002-108843	20020327
PRIORITY APPLN. INFO.:			US 2001-279214P	P 20010328

OTHER SOURCE(S): MARPAT 137:310928

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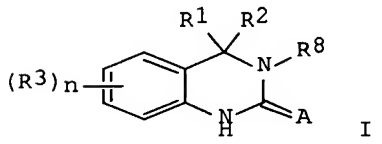

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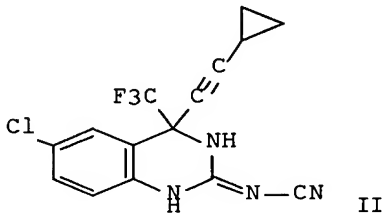


II

AB Title compds. I [A = NCN, NCONH, NOR9; R1 = haloalkyl; R2 = alk(en/yn)yl; R3 = alkyl, OH, alkoxy, F, Cl, Br, I, amino, NO2, CN, etc. or alternatively, if two R3 are present and are attached to adjacent carbons, then they may combine to form -OCH2O-; R8 = H, cycloalkyl, alkyl, phenyl; R9 = H, alkyl; n = 0-4] were prepared A substituted quinolin-2-one was converted to the imidoyl chloride (mixture, POCl3, 95°, 16 h) and treated with cyanamide (70°, 8 h; EtOH, reflux) which afforded II as a white solid. I, alone and in combination with HIV reverse transcriptase inhibitors, are useful for treating HIV infection.

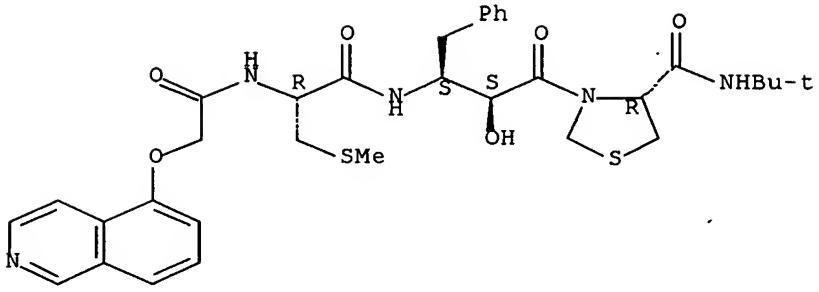
IT **147318-81-8**, KNI-272

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of cyanamide, alkoxyamino, and urea
quinazolin-2-one derivs. as HIV reverse transcriptase **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

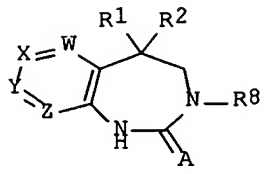


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

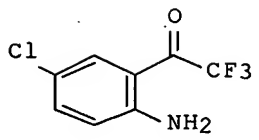
L31 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:777651 HCAPLUS Full-text
DOCUMENT NUMBER: 137:294988
TITLE: Cyanamide, alkoxyamino, and urea derivatives of 1,3-benzodiazapines as HIV reverse transcriptase inhibitors
INVENTOR(S): Bilder, Donna M.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078628	A2	20021010	WO 2002-US9456	20020327 <--
WO 2002078628	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003220327	A1	20031127	US 2002-108842	20020327
PRIORITY APPLN. INFO.:			US 2001-279217P P	20010328

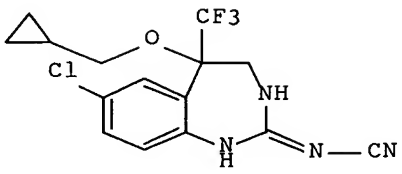
OTHER SOURCE(S): MARPAT 137:294988
GI



I



II



III

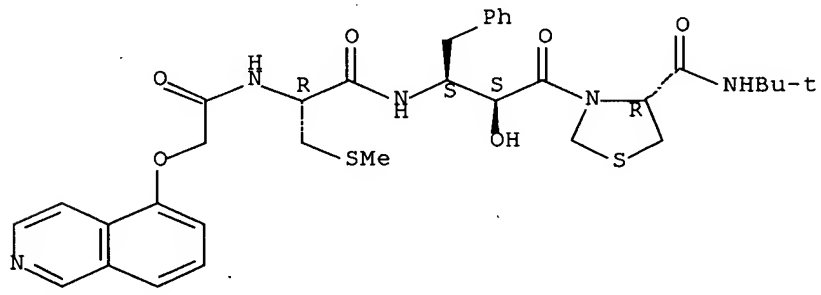
AB Title compds. I [A = NCN, NCONH, N-alkoxy; W = N, CR3; X = N, CR3a; Y = N, CR3b; Z = N, CR3c; provided that if two of W, X, Y, and Z are N, then the remaining are other than N; R1 = alkyl; R2 = R2c, OR2c, etc.; R2c = alk(en/yn)yl, cycloalkyl, Ph, etc.; R3 = H, alkyl, OH, alkoxy, OCF3, etc.; R3a = H, alkyl, OH, alkoxy, OCF3, F, Cl, Br, etc.; R3b = H, alkyl, OH, alkoxy, OCF3, F, Cl, Br, etc.; R3c = H, alkyl, OH, alkoxy, OCF3, F, Cl, Br, etc.; R8 = H, alkoxy, thioalkoxy, amino, alkyl, etc.] were prepared For instance, II was subjected to the following sequence: i. DMSO/THF, Me3SOI, NaH; ii. EtOH, NH3, 45°, 2 days; iii. IPA, diphenylcyanocarbonimidate; iv. DMSO, NaH, BrCH2Pr-c to afford III. I are useful as inhibitors of HIV reverse transcriptase, and to pharmaceutical compns. and diagnostic kits comprising the same, and methods of using the same for treating viral infection or as an assay standard or reagent.

IT **147318-81-8**, KNI-272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; cyanamide, alkoxyamino, and urea derivs. of 1,3-benzodiazapines as HIV reverse transcriptase **inhibitors**
)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:736212 HCAPLUS Full-text

DOCUMENT NUMBER: 137:242144
TITLE: Allophenylnorstatine-based inhibitors of plasmepsins, and use in the treatment of malaria and inhibition of cathepsin D
INVENTOR(S): Freire, Ernesto; Nezami, Azin; Koso, Yoshiaki
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074719	A2	20020926	WO 2002-US8024	20020315 <--
WO 2002074719	C1	20030313		
WO 2002074719	A3	20040521		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005037953	A1	20050217	US 2004-471655		20040910
PRIORITY APPLN. INFO.:			US 2001-275713P	P	20010315
			WO 2002-US8024	W	20020315

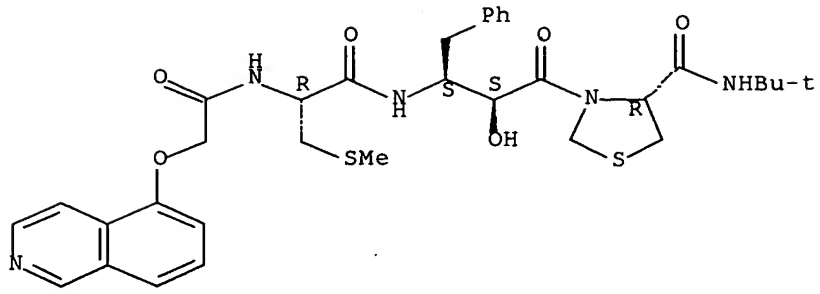
OTHER SOURCE(S): MARPAT 137:242144

AB Compds. and methods for the inhibition of antimalarial target aspartyl protease plasmepsins (e.g. Plasmepsin I, Plasmepsin II, Plasmepsin IV and HAP) are provided. The compds. are allophenylnorstatine-based derivs. and may be used to inhibit Plasmepsin II, to kill malarial parasites, and to treat malaria in a patient. Certain of the substituted allophenylnorstatine-based compds. also exhibit inhibitory activity against Cathepsin D.

IT **147318-81-8**, KNI 272 **147384-69-8**, KNI 227
225377-99-1, KNI 529 **324522-52-3**, KNI 492
461015-52-1 **461444-57-5**, KNI 10033 **461444-79-1**
, KNI 10032 **461444-80-4**, KNI 10042 **461444-86-0**, KNI 10050 **461444-87-1**, KNI 10051 **461444-90-6**, KNI 10055
461444-92-8, KNI 10057
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(allophenylnorstatine-based **inhibitors** of plasmepsins, and use in treatment of malaria and **inhibition** of cathepsin D)

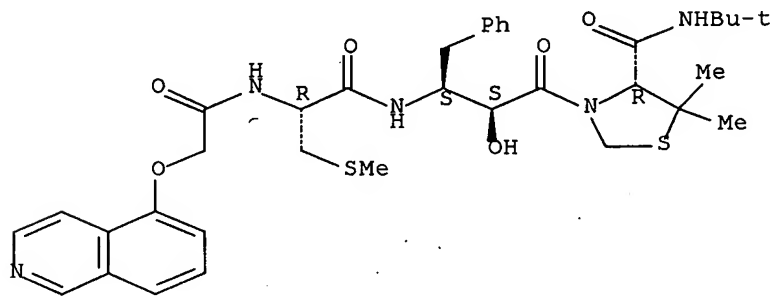
RN 147318-81-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



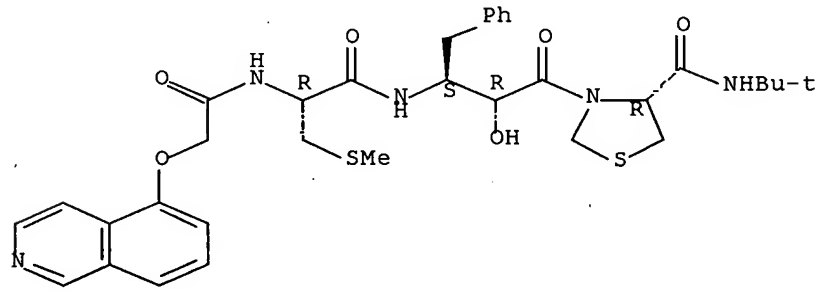
RN 147384-69-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



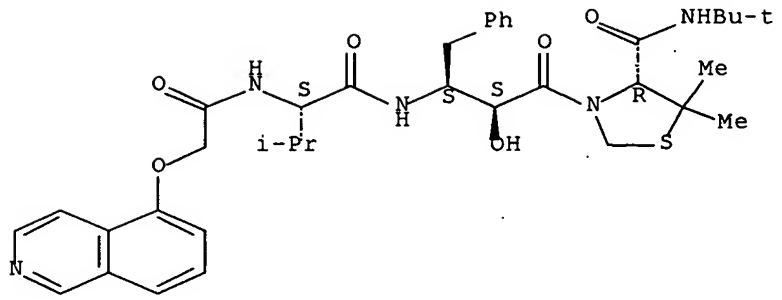
RN 225377-99-1 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2R,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



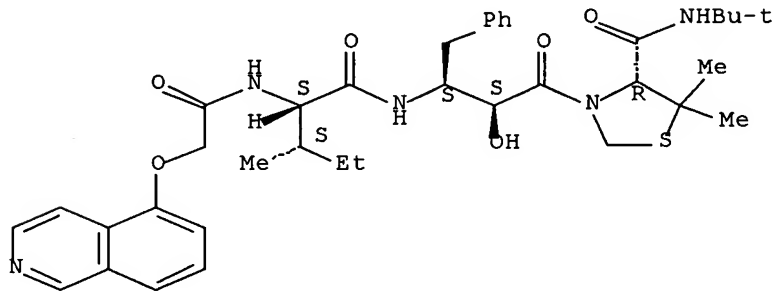
RN 324522-52-3 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-1-oxobutyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



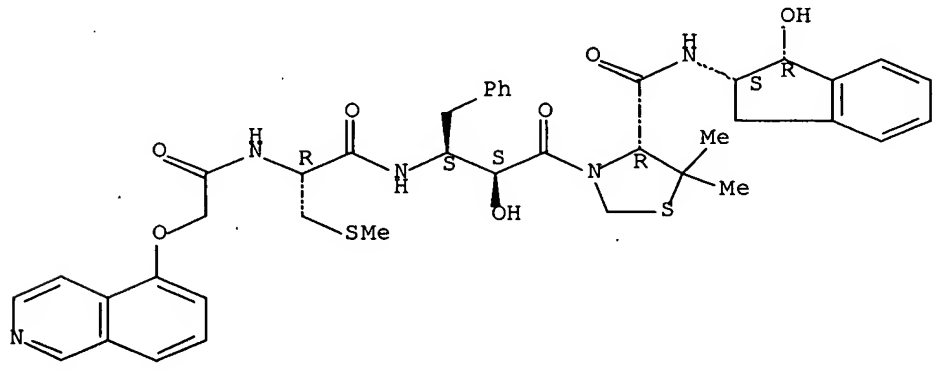
RN 461015-52-1 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S,3S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-1-oxopentyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



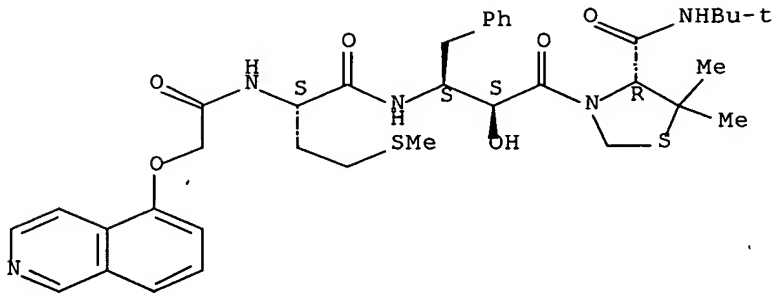
RN 461444-57-5 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-[(1R,2S)-2,3-dihydro-1-hydroxy-1H-inden-2-yl]-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



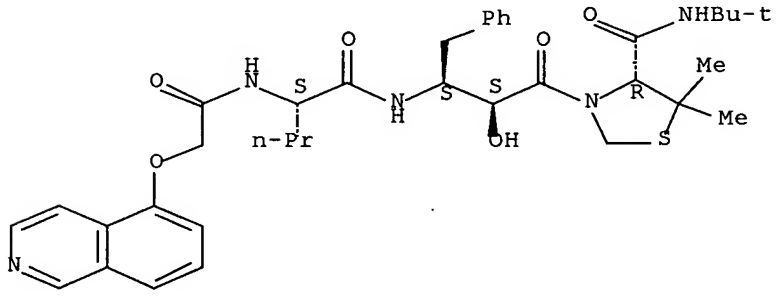
RN 461444-79-1 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-4-(methylthio)-1-oxobutyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



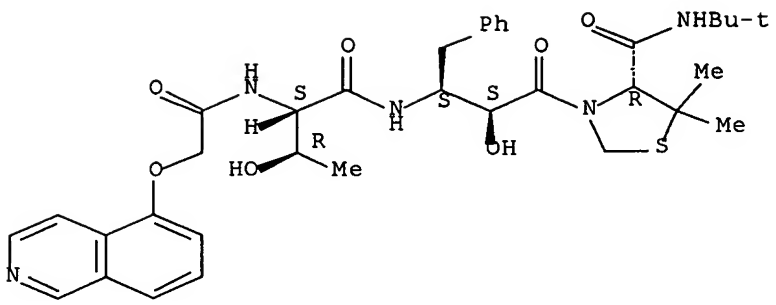
RN 461444-80-4 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-1-oxopentyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



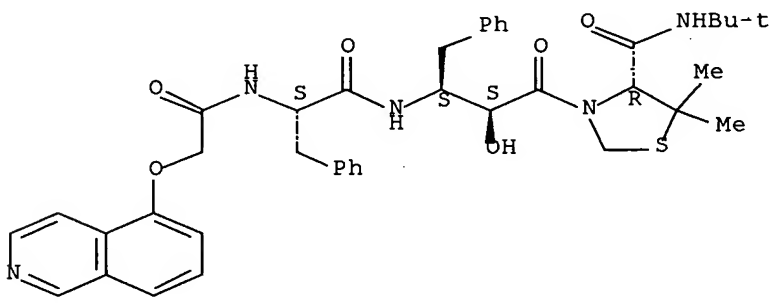
RN 461444-86-0 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S,3R)-3-hydroxy-2-[[(5-isoquinolinyloxy)acetyl]amino]-1-oxobutyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



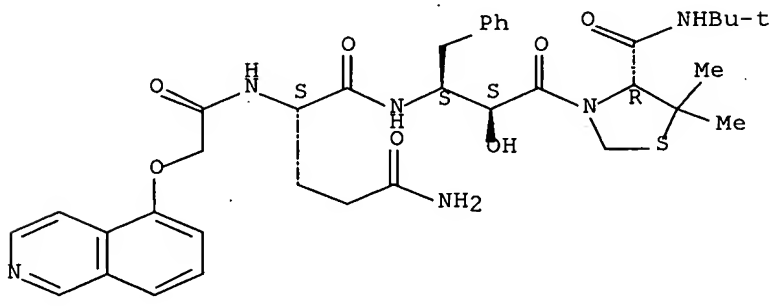
RN 461444-87-1 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-1-oxo-3-phenylpropyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



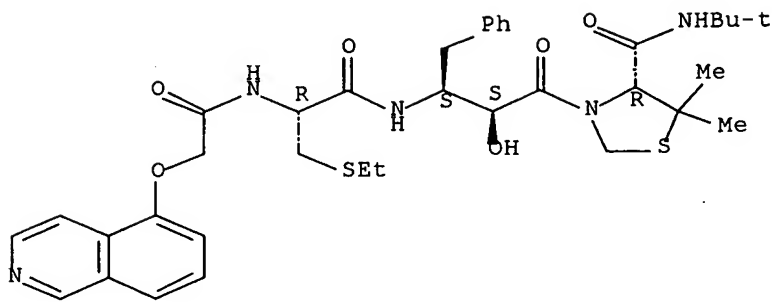
RN 461444-90-6 HCAPLUS
CN Pentanediamide, N1-[(1S,2S)-3-[(4R)-4-[[(1,1-dimethylethyl)amino]carbonyl]-5,5-dimethyl-3-thiazolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-[[(5-isoquinolinyloxy)acetyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 461444-92-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-3-[[(2R)-3-(ethylthio)-2-[[(5-isoquinolinyloxy)acetyl]amino]-1-oxopropyl]amino]-2-hydroxy-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:695941 HCAPLUS Full-text
DOCUMENT NUMBER: 137:232453
TITLE: Preparation of substituted benzophenones as inhibitors of reverse transcriptase
INVENTOR(S): Chan, Joseph Howing
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070470	A2	20020912	WO 2002-US6037	20020228 <--
WO 2002070470	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439820	AA	20020912	CA 2002-2439820	20020228 <--
EP 1363877	A2	20031126	EP 2002-723265	20020228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007752	A	20040323	BR 2002-7752	20020228
NZ 527864	A	20040528	NZ 2002-527864	20020228
JP 2004525914	T2	20040826	JP 2002-569791	20020228
NO 2003003857	A	20031027	NO 2003-3857	20030901
US 2004122064	A1	20040624	US 2004-469104	20040205
PRIORITY APPLN. INFO.:			US 2001-272953P	P 20010302
			WO 2002-US6037	W 20020228

OTHER SOURCE(S): MARPAT 137:232453
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

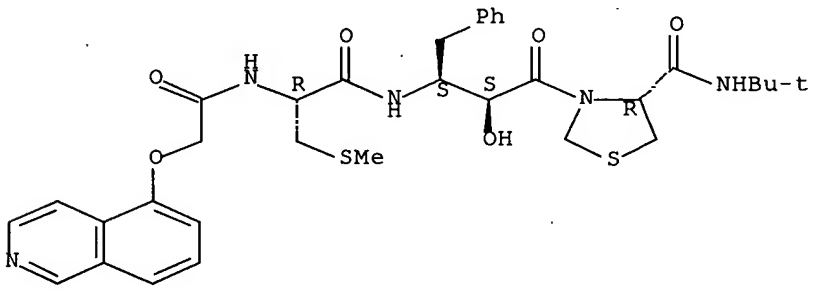
AB Title compds. I [R1 = ≥1 substituent chosen from halo, CF3, alkyl, aminoalkyl, alkoxy, CN, NO2, NH2, thioalkoxy, etc.; R2 = H, halo, alkyl, NO2, NH2, alkylamino, CF3, alkoxy; R3 = OH, halo, CF3, NO2, alkyl; R4 = sulfonamido, sulfonylimino, etc.;] were prepared For instance, 3,5-dichlorobromobenzene was metalated (MTBE, n-BuLi, -50°) and acylated with the N,2-dimethoxy-N-methyl-5-chlorobenzamide and the resulting benzophenone converted to II. II was converted to III in 5 steps. Polymorphic forms of sodium, choline, calcium, magnesium, ethanolamine and triethylamine salts of III were prepared and characterized. Oral bioavailability and solubility parameters were determined for III and polymorphic salt forms thereof. Compds. of the present invention have anti-HIV activity and deliver compds. that have anti- HIV activity in the range IC50 = 1-1000 nM against wild type and mutant viruses.

IT **147318-81-8**, KNI-272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of substituted benzophenones as **inhibitors** of reverse transcriptase)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

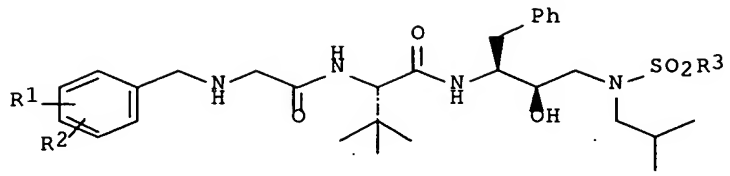
Absolute stereochemistry.



L31 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:387597 HCAPLUS Full-text
DOCUMENT NUMBER: 136:370003
TITLE: Preparation of bis-amino acid sulfonamides containing substituted benzyl amines as HIV protease inhibitors
INVENTOR(S): Kaltenbach, Robert F.; Trainor, George L.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Pharmaceutical Company, USA
SOURCE: U.S., 22 pp.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6391919	B1	20020521	US 2000-482146	20000112 <--
PRIORITY APPLN. INFO.:			US 2000-482146	20000112
OTHER SOURCE(S):	MARPAT 136:370003			

GI



I

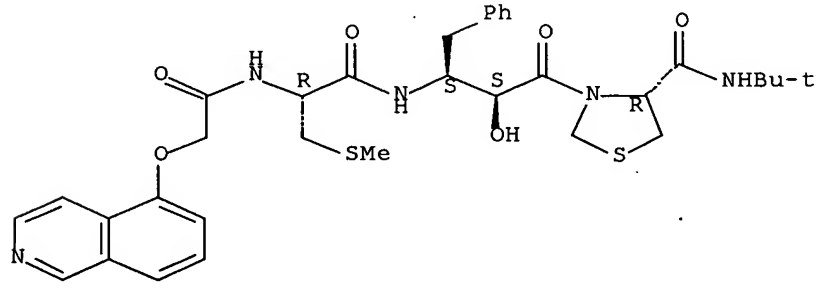
AB Title compds. I (R1 = F; R2 = H, F; R3 = 3- or 4-aminophenyl, 2,3-dihydrobenzofuran-5-yl, 1,3-benzodioxol-5-yl) were prepared as HIV protease inhibitors. Thus, I (R1 = 3-F; R2 = H; R3 = 4-aminophenyl) was prepared by a multistep procedure starting from N-[3(S)- [bis(phenylmethyl)amino]-2(R)-hydroxy-4-phenylbutyl]-N-isobutylamine oxalate salt.

IT **147318-81-8**, KNI-272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of bis-amino acid sulfonamides containing substituted benzyl amines
as HIV protease **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:276520 HCAPLUS Full-text

DOCUMENT NUMBER: 136:310189

TITLE: Preparation of C-terminal modified oxamyl dipeptides as inhibitors of the ICE/ced-3 family of cysteine proteases

INVENTOR(S): Karanewsky, Donald S.; Ternansky, Robert J.; Linton, Steven D.; Dinh, Thang

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 745,204.
CODEN: USXXCO

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002042376	A1	20020411	US 2001-765105	20010116 <--
US 6197750	B1	20010306	US 1998-177549	19981022 <--
US 2002028774	A1	20020307	US 2000-745204	20001219 <--
US 6544951	B2	20030408		
ZA 2001000023	A	20020102	ZA 2001-23	20010102 <--
CA 2433879	AA	20020725	CA 2002-2433879	20020116 <--
WO 2002057298	A2	20020725	WO 2002-US1538	20020116 <--
WO 2002057298	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1351975	A2	20031015	EP 2002-705856	20020116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521107	T2	20040715	JP 2002-557974	20020116
US 2005020504	A1	20050127	US 2004-926800	20040825

PRIORITY APPLN. INFO.:		
US 1998-91689P	P	19980702
US 1998-177549	A2	19981022
US 2000-745204	A2	20001219
WO 1999-US15074	A1	19990701
US 2001-765105	A	20010116
WO 2002-US1538	W	20020116

OTHER SOURCE(S): MARPAT 136:310189

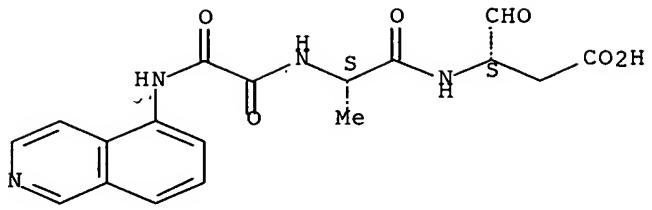
AB Oxamyl dipeptides R1R1'NCOCO-A-NHCH(CO-B)CH2CO2R2 [A is a natural or unnatural amino acid; B = H, D, alkyl, cycloalkyl, (un)substituted Ph or naphthyl, 2-benzoxazolyl, substituted 2-oxazolyl, (CH2)ncycloalkyl, (CH2)nphenyl, (CH2)n(1- or 2-naphthyl), (CH2)nheteroaryl (n = 1-4), etc.; R1 = alkyl, cycloalkyl, cycloalkylalkyl, (un)substituted Ph, phenylalkyl, or naphthyl, etc. or R1R1'N form a heterocycle; R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, (un)substituted Ph, phenylalkyl, naphthyl, or naphthylalkyl] were prepared as inhibitors of the ICE/ced-3 family of cysteine proteases (ICE = interleukin-1β converting enzyme). Thus, (3S)-3-[[N-(1-naphthyloxamyl)leucinyl]amino]-4-oxobutanoic acid was prepared via coupling of 1-naphthyloxamic acid with (3S)-3-(leucinylamino)-4- oxobutanoic acid tert-Bu ester semicarbazone.

IT **409368-91-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of C-terminal modified oxamyl dipeptides as **inhibitors** of ICE/ced-3 family of cysteine proteases)

RN 409368-91-8 HCAPLUS

CN L-Alaninamide, N-5-isoquinolinyl-2-oxoglycyl-N-[(1S)-2-carboxy-1-formylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

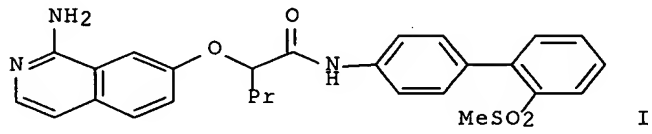


L31 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:240733 HCAPLUS Full-text
DOCUMENT NUMBER: 136:263103
TITLE: Biphenyl-substituted aminoquinolines and -isoquinolines as factor Xa inhibitors
INVENTOR(S): Dorsch, Dieter; Juraszyk, Horst; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024654	A1	20020328	WO 2001-EP10786	20010918 <--
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10046272	A1	20020328	DE 2000-10046272	20000919 <--
CA 2422067	AA	20030312	CA 2001-2422067	20010918
EP 1322618	A1	20030702	EP 2001-985251	20010918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004513888	T2	20040513	JP 2002-529067	20010918

PRIORITY APPLN. INFO.: DE 2000-10046272 A 20000919
WO 2001-EP10786 W 20010918

OTHER SOURCE(S): MARPAT 136:263103
GI



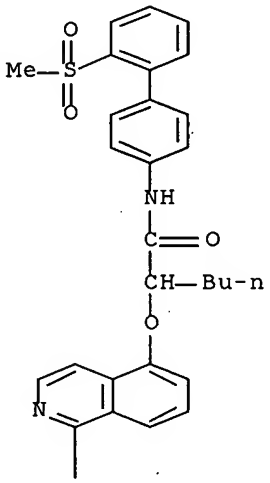
I

AB The title compds. were prepared for use as inhibitors of blood coagulation factors Xa and VIIa (no data). Thus, 7-isoquinolinol was treated with BrCHPrCO2CMe3, followed by ester hydrolysis, amidation with 2-MeSO2C6H4C6H4NH2-4, N-oxidation, reaction with pyridine, and treatment with ethanolamine to give the title compound I.

IT **405272-17-5P 405272-18-6P 405272-19-7P 405272-20-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of biphenyl-substituted aminoquinolines and -isoquinolines as factor Xa **inhibitors**)

RN 405272-17-5 HCAPLUS
CN Hexanamide, 2-[(1-amino-5-isoquinolinyl)oxy]-N-[2'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)

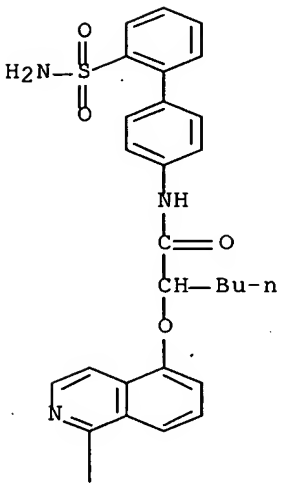
PAGE 1-A



PAGE 2-A

RN 405272-18-6 HCAPLUS
CN Hexanamide, 2-[(1-amino-5-isoquinolinyl)oxy]-N-[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)

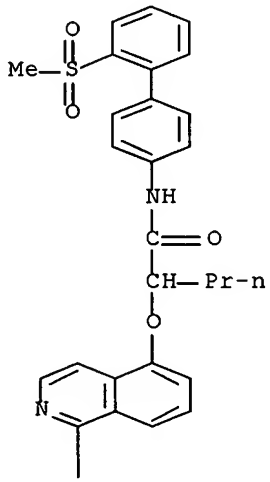
PAGE 1-A



PAGE 2-A

RN 405272-19-7 HCAPLUS
CN Pentanamide, 2-[(1-amino-5-isoquinolinyl)oxy]-N-[2'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

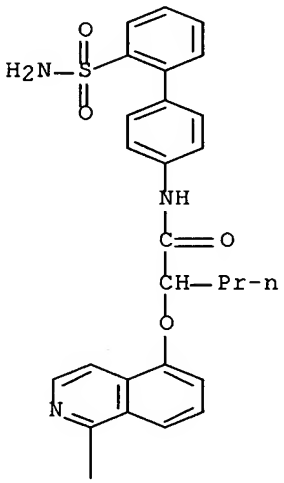


PAGE 2-A

NH2

RN 405272-20-0 HCAPLUS
CN Pentanamide, 2-[(1-amino-5-isoquinolinyl)oxy]-N-[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

NH2

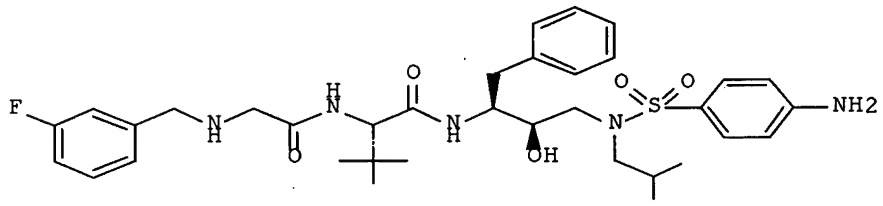
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:107305 HCAPLUS Full-text
DOCUMENT NUMBER: 136:172757
TITLE: Salt forms of an HIV protease inhibitor
INVENTOR(S): Harris, Gregory D.; Anderson, Stephen R.; Desikan, Sridhar; Meenan, Paul A.; Stone, Benjamin R.; Toma, Pascal H.
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002010124 A2 20020207 WO 2001-US22810 20010719 <--
WO 2002010124 A3 20030501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002022742 A1 20020221 US 2001-908126 20010718 <--
PRIORITY APPLN. INFO.: US 2000-219794P P 20000729

GI



I

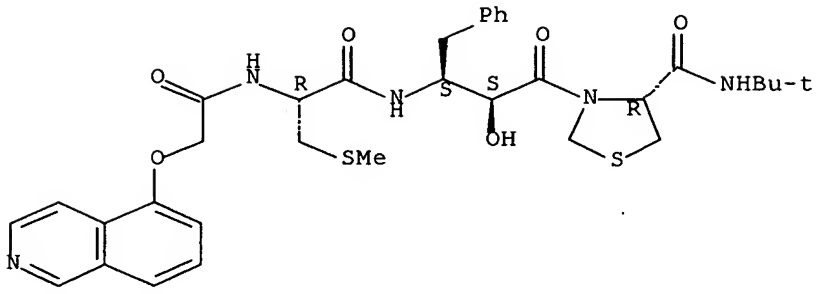
AB An HIV protease inhibitor (I) and its salt forms, i.e., mono-fumarate, mono-camphor sulfonate, mono-methane sulfonate, mono-phosphate, and bis-toluene sulfonate, are prepared for pharmaceutical kits useful for treating HIV viral infections. Pharmaceutical kits comprise (a) a salt of I and (b) at least one compound selected from HIV reverse transcriptase inhibitors, such as AZT, efavirenz, and 3TC, and other HIV protease inhibitors, such as saquinavir, ritonavir, nelfinavir and indinavir. Component (a) and component (b) may be sep. or phys. combined into a single dosage form, e.g., a capsule, a suspension, or a parenteral compn.

IT **147318-81-8**, KNI-272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and formulation of salt forms of HIV protease **inhibitor** for treatment of HIV viral infections)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:90044 HCAPLUS Full-text
DOCUMENT NUMBER: 136:151150
TITLE: Tricyclic 2-pyridone compounds useful as HIV reverse transcriptase inhibitors and their use as antiviral agents in the treatment of HIV infection
INVENTOR(S): Rodgers, James D.; Wang, Haisheng; Patel, Mona; Arvanitis, Argyrios; Cocuzza, Anthony J.
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008226	A2	20020131	WO 2001-US22827	20010720 <--
WO 2002008226	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002107261	A1	20020808	US 2001-908995	20010719 <--
US 6596729	B2	20030722		
CA 2418194	AA	20020131	CA 2001-2418194	20010720 <--
EP 1303515	A2	20030423	EP 2001-959047	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
SI 21139	C	20030831	SI 2001-20050	20010720
BR 2001012606	A	20040629	BR 2001-12606	20010720
EE 200300027	A	20041015	EE 2003-27	20010720
JP 2004532793	T2	20041028	JP 2002-514132	20010720
BG 107439	A	20030930	BG 2003-107439	20030106
ZA 2003000255	A	20040928	ZA 2003-255	20030109
NO 2003000248	A	20030317	NO 2003-248	20030117
US 2004023955	A1	20040205	US 2003-457902	20030610
PRIORITY APPLN. INFO.:			US 2000-219532P	P 20000720
			US 2001-284856P	P 20010419
			US 2001-908995	A3 20010719

WO 2001-US22827 W 20010720

OTHER SOURCE(S): MARPAT 136:151150

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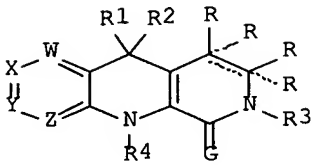

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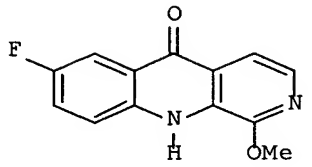
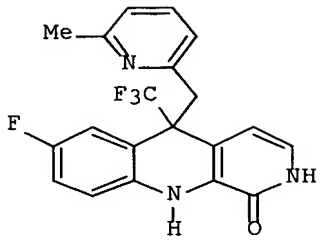


II



III

AB The invention relates to tricyclic 2-pyridone compds. I or stereoisomeric forms, stereoisomeric mixts., or pharmaceutically acceptable salt forms thereof [wherein: G = O or S; W, X, Y, Z = N or (un)substituted CH (if 2 of them are N, the others are not); R1 = C1-4 alkyl substituted with 0-9 halo, cyclopropyl, hydroxymethyl, or cyano; R2 = (un)substituted alk(en/yn)yl, cycloalkyl, Ph, or heterocyclyl; R's = (independently) H, halo, cyano, alk(en/yn)yl, alkoxy, alkylamino, NH2, depending upon position and presence or absence of double bond; R3 = H, alk(en/yn)yl, alkoxy, alkanoyl, aryloxy, alkoxycarbonyl, etc.; R4 = H, alkanoyl, alkoxy, alkoxycarbonyl, aryloxy, etc.]. The compds. are useful as inhibitors of HIV reverse transcriptase. The invention also relates to pharmaceutical compns. and diagnostic kits comprising the compds., and methods of using them for treating viral infection, or as an assay standard or reagent. The compds. may be used in combination with a variety of other HIV reverse transcriptase inhibitors, HIV protease inhibitors, fusion inhibitors, and CCR-5 inhibitors. Of many specifically disclosed compds. for such combination use, AZT and indinavir are particularly claimed. Well over 100 specific examples of I were prepared and/or individually claimed. For instance, the intermediate 7-fluoro-1-methoxybenzo[b]-1,7-naphthyridin- 5(10H)-one (II) was prepared in 3 steps. This compound underwent N-protection with SEM-Cl (96%), trifluoromethylation with CF3-TMS, deprotection with TFA (93%), coupling with lithiated 2,6-lutidine (13%), and demethylation of the Me ether (79%), to give title compound III. A number of compds. I exhibited Ki values of ≤ 10 μM in an HIV reverse transcriptase bioassay.

IT **147318-81-8**

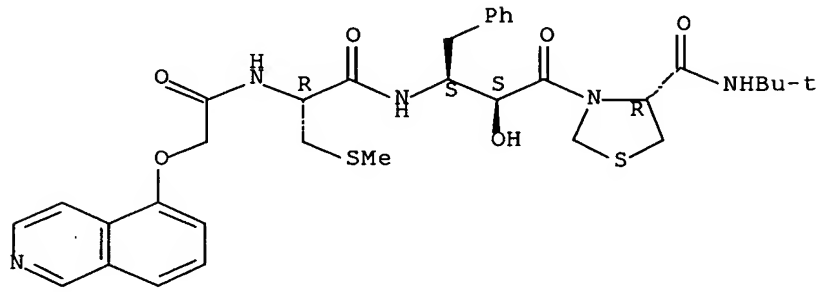
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. also containing; preparation of tricyclic 2-pyridone
compds. as HIV reverse transcriptase **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-

oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:72008 HCAPLUS Full-text
DOCUMENT NUMBER: 136:135026
TITLE: Crystalline and salt forms of an hiv protease inhibitor
INVENTOR(S): Harris, Thomas D.; Anderson, Stephen R.; Desikan, Sridhar; Meenan, Paul A.; Stone, Benjamin R.; Toma, Pascal H.; Deshmukh, Subodh Shrinivas
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006190	A2	20020124	WO 2001-US22812	20010719 <--
WO 2002006190	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002022659	A1	20020221	US 2001-908430	20010718 <--
AU 2001080636	A5	20020130	AU 2001-80636	20010719 <--
PRIORITY APPLN. INFO.:			US 2000-219390P P	20000719
			WO 2001-US22812 W	20010719

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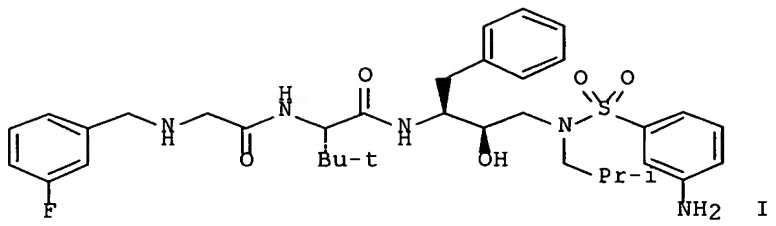


I

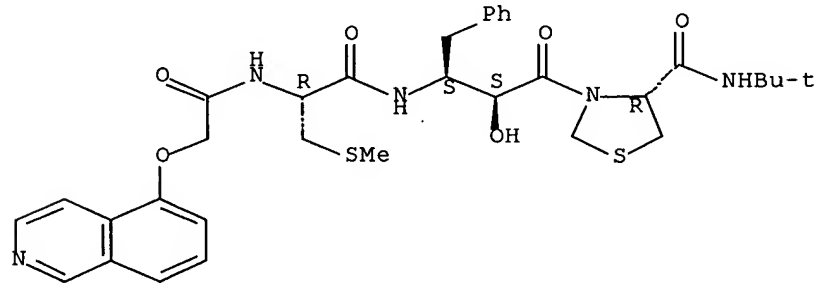
AB This invention relates to crystalline and salt forms of compds. of formula I that are useful as HIV protease inhibitors for treating viral infection. Examples include the synthesis and characterization of I, a mesylate (forms I and II), bis-mesylate (forms I and II), hydrate, several solvates, p-toluenesulfonate and phosphate of I. Polymorphs were characterized by x-ray diffraction anal. and differential scanning calorimetry.

IT **147318-81-8**, KNI-272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; crystalline and salt forms of an hiv protease **inhibitor**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:923790 HCAPLUS Full-text

DOCUMENT NUMBER: 136:53748

TITLE: Preparation of propenone derivatives as integrase inhibitors and synergistic medicinal compositions containing them and anti-retrovirus agents

INVENTOR(S): Sato, Akihiko

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan

SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001096329 A1 20011220 WO 2001-JP4887 20010611 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001062733 A5 20011224 AU 2001-62733 20010611 <--
CA 2410763 AA 20021128 CA 2001-2410763 20010611
EP 1295879 A1 20030326 EP 2001-936940 20010611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
BR 2001011678 A 20030603 BR 2001-11678 20010611
US 2003171406 A1 20030911 US 2002-296475 20021125
ZA 2002009673 A 20040420 ZA 2002-9673 20021128
NO 2002006013 A 20030213 NO 2002-6013 20021213
PRIORITY APPLN. INFO.: JP 2000-176844 A 20000613
WO 2001-JP4887 W 20010611

OTHER SOURCE(S): MARPAT 136:53748

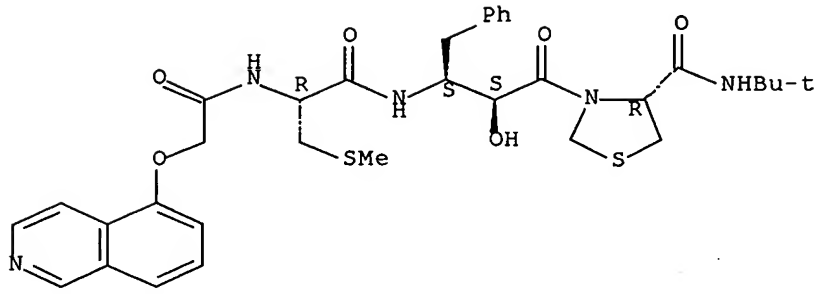
AB Described is a combination of an integrase inhibitor with an anti-retrovirus active substance and medicinal compns. containing the same as the active ingredients. The above integrase inhibitors are represented by formula A-CO-CH:(OH)-B [A = (un)substituted heteroaryl; B = (un)substituted heteroaryl or aryl; provided that compds. represented by A and/or B = (un)substituted indol-3-yl are excluded.], tautomers, prodrugs, or pharmaceutically acceptable salts thereof and prepared The anti-retrovirus active substances are zidovudine, didanosine, zalcitabine, stavudine, lamivudine, abacavir, tenofovir, tenofovir disproxil, nevirapine, delavirdine, emivirine, loviride, efavirenz, trovirdine, capravirine, TIBO, talviraline, UC781, saquinavir, nelfinavir, ritonavir, indinavir, KNI-272, lopinavir, VX-478, VB-19026, BILA-2011-BS, A-77003, A-80987, DMP-323, and XM-450. Thus, a THF solution of 1.31 g 2-acetyl-5-(4-fluorobenzyl)furan (18 ML) was cooled, treated dropwise with a 1 M lithium trimethylsilylamide solution in THF (7.8 mL) at -70 to -65°, gradually warmed to -10°, cooled to -70°, treated with a THF solution of 2.99 g 1-trityl-1H-1,2,4-triazole-3-carboxylic acid Et ester (30 mL), gradually warmed to room temperature, and stirred for 1.5 h, followed by work-up and treatment of the product with a mixture of 1 M aqueous HCl and dioxane at 80° for 0.5 h, and further work-up, to give 1-[5-(4-fluorobenzyl)furan-2-yl]-3-hydroxy-3-(1H-1,2,4-triazol-3-yl)-2- propen-1-one (I). I and 1-[2-(4-fluorobenzyl)furan-3-yl]-3-hydroxy-3-(2H- tetrazol-5-yl)-2-propen-1-one showed IC50 of 0.53 and 0.32 μg/mL, resp., against HIV-1 integrase. I in combination of zidovudine, lamivudine, nevirapine, capravirine, or nelfinavir showed synergism for inhibiting HIV-1 in MT-4 cells.

IT **147318-81-8**, KNI-272
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(anti-retrovirus synergistic composition; preparation of propenone derivs. as integrase **inhibitors** and synergistic medicinal compns. containing them and anti-retrovirus agents)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:833091 HCAPLUS Full-text
DOCUMENT NUMBER: 135:352765
TITLE: Peptide deformylase (PDF) inhibitors, and their use in the treatment of bacterial infections
INVENTOR(S): Aubart, Kelly M.; Christensen, Siegfried B., IV; Briand, Jacques
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085170	A1	20011115	WO 2001-US14593	20010504 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2408236	AA	20011115	CA 2001-2408236	20010504 <--
BR 2001010206	A	20030128	BR 2001-10206	20010504
EP 1283711	A1	20030219	EP 2001-935094	20010504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003532677	T2	20031105	JP 2001-581824	20010504
NZ 521560	A	20040528	NZ 2001-521560	20010504
ZA 2002008909	A	20031016	ZA 2002-8909	20021101
NO 2002005281	A	20030103	NO 2002-5281	20021104
US 2004053932	A1	20040318	US 2002-275522	20021105
US 6806369	B2	20041019		
US 2004192719	A1	20040930	US 2004-818074	20040405
PRIORITY APPLN. INFO.:			US 2000-201943P P	20000505
			US 2000-238084P P	20001004
			WO 2001-US14593 W	20010504
			US 2002-275522 A3	20021105

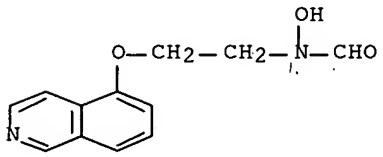
OTHER SOURCE(S): MARPAT 135:352765

AB PDF inhibitors and methods for their use are provided. The PDF inhibitors include ArX(CH2)nCH2N(OH)C(O)H (X = O; n = 1, 2; Ar = aryl group). Compds. of the invention include e.g. N-formyl-N-hydroxy-4- phenylbutylamine. The PDF inhibitors can potentially serve as broad-spectrum antibacterial agents.

IT **372947-35-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide deformylase **inhibitors**, and use in treatment of bacterial infection)

RN 372947-35-8 HCAPLUS

CN Formamide, N-hydroxy-N-[2-(5-isoquinolinyloxy)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:429534 HCAPLUS Full-text
DOCUMENT NUMBER: 135:33651
TITLE: Preparation of peptides as efflux pump inhibitors
INVENTOR(S): Chamberland, Suzanne; Lee, May; Leger, Roger; Lee, Ving J.; Renau, Thomas; Zhang, Zhijia J.
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: U.S., 48 pp., Cont.-in-part of U.S. 6,114,310.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6245746	B1	20010612	US 1998-20001	19980204 <--
US 6114310	A	20000905	US 1998-12363	19980123 <--
WO 9937667	A1	19990729	WO 1999-US1422	19990122 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9923375	A1	19990809	AU 1999-23375	19990122 <--

PRIORITY APPLN. INFO.:

US 1998-12363	A2	19980123
US 1998-20001	A	19980204
US 1998-89734	A	19980603
WO 1999-US1422	W	19990122

OTHER SOURCE(S): MARPAT 135:33651

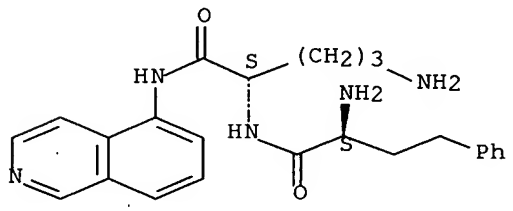
AB Compds. RCHW-CO-NR2-CHR1-M-P-S-X [M = (CH2)n (n = 0, 1, 2); P = CH2, CO, CS; S = NH, O, SOt (t = 0, 1, 2); R, R1, R2 independently = alkyl, fluoroalkyl, aryl, thienyl, furyl, pyridyl, etc.; W = (α- aminoacyl)amido, aminoalkyl, NH2, (un)substituted azaheterocyclyl, OH, alkoxy, alkylthio, guanidino, amidino, or halogen; X = aryl, thienyl, furyl, pyridyl, indanyl, quinolyl, etc.] were prepared as efflux pump inhibitors which increase the susceptibility of microbes to antimicrobial agents. In vitro microbiol. data for antibiotic potentiation are tabulated for 195 compds., including phenylalanyl-ornithine quinoline-3-amide.

IT **233686-65-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as efflux pump **inhibitors**)

RN 233686-65-2 HCAPLUS

CN Benzenebutanamide, α-amino-N-[(1S)-4-amino-1-[(5-isoquinolinylamino)carbonyl]butyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

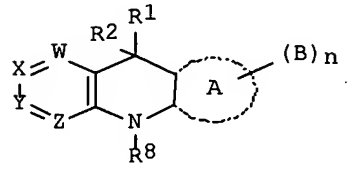
L31 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:300717 HCAPLUS Full-text
DOCUMENT NUMBER: 134:326518
TITLE: Preparation of tricyclic compounds useful as HIV reverse transcriptase inhibitors
INVENTOR(S): Johnson, Barry L.; Patel, Mona; Rodgers, James D.; Wang, Haisheng
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 230 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029037	A2	20010426	WO 2000-US28824	20001019 <--
WO 2001029037	A3	20020124		
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6593337	B1	20030715	US 2000-691249	20001018
CA 2387896	AA	20010426	CA 2000-2387896	20001019 <--

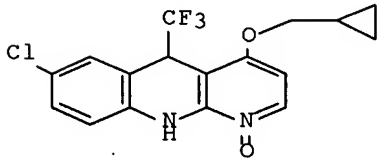
EP 1222186	A2	20020717	EP 2000-973644		20001019 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003512375	T2	20030402	JP 2001-531836		20001019
ZA 2002003131	A	20030422	ZA 2002-3131		20001019
BR 2000015056	A	20030610	BR 2000-15056		20001019
EE 200200202	A	20030616	EE 2002-202		20001019
AU 773309	B2	20040520	AU 2001-12137		20001019
NO 2002001835	A	20020618	NO 2002-1835		20020418 <--
US 2004002498	A1	20040101	US 2003-422202		20030424
PRIORITY APPLN. INFO.:			US 1999-160329P	P	19991019
			US 2000-226171P	P	20000817
			US 2000-691249	A3	20001018
			WO 2000-US28824	W	20001019

OTHER SOURCE(S): MARPAT 134:326518

GI



I



II

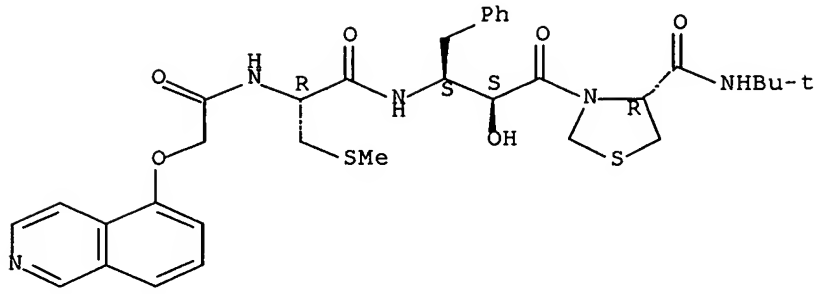
AB Title compds. [I; n = 0, 1, 2, 3; A = heterocycle; B = alkyl, OH, alkoxy, OCF3, CF3, F, Cl, Br, I, NO2, CN; W = N, CR3; X = N, CR3a; Y = N, CF3b; Z = N, CR3c; R3, R3a-R3c independently = H, alkyl, OH, OCF3, helo, CN; R1 = alkyl, cyclopropyl; R2 = OH, CN, alkoxy, alkylamino; R8 = H, alkylcarbonyl, alkoxyalkyl, aryloxyalkyl], stereoisomers, stereoisomers mixts., or pharmaceutically acceptable salts are prepared as useful inhibitors of HIV reverse transcriptase. Pharmaceutical compns. and diagnostic kits comprising title compds. and methods for treating viral infections or as an assay standard or reagent were discussed. Thus, the title compound II was prepared

IT **147318-81-8**, KNI-272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV protease **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:628160 HCAPLUS Full-text
DOCUMENT NUMBER: 133:232870
TITLE: Inhibitors of serine protease activity, and methods and compositions for treatment of viral infections and other conditions
INVENTOR(S): Shapiro, Leland
PATENT ASSIGNEE(S): The Trustees of University Technology Corp., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052034	A2	20000908	WO 2000-US5558	20000303 <--
WO 2000052034	A3	20010111		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6849605	B1	20050201	US 2000-518098	20000303
PRIORITY APPLN. INFO.:			US 1999-123167P	P 19990305
			US 1999-137795P	P 19990603

OTHER SOURCE(S): MARPAT 133:232870

AB A method of treating and preventing viral infection is provided. In particular, a method of blocking viral infection facilitated by a serine proteolytic activity is disclosed, which consists of administering to a subject suffering or about to suffer from viral infection a therapeutically effective amount of a compound having a serine protease inhibitory or serpin activity. Among compds. are α1-antitrypsin (AAT), peptide derivs. from the carboxyterminal end of AAT, and man-made, synthetic compds. mimicking the action of such compds. The preferred viral infections include retroviral infection such as human immunodeficiency virus (HIV) infection. A method for treating other pathol. conditions mediated my a serine protease is also disclosed.

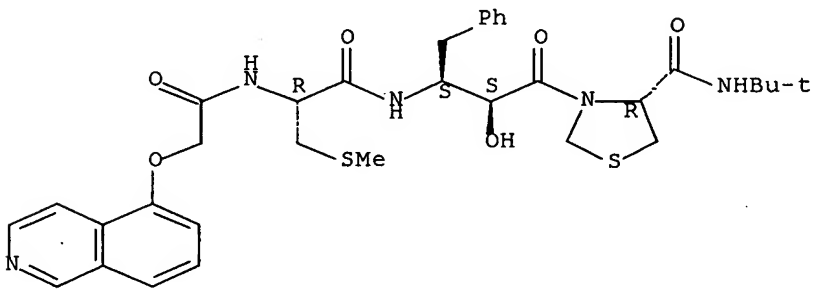
IT **147318-81-8**, KNI-272
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(serine protease **inhibitors** for treatment of viral infections and other conditions, and use with other agents)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:362575 HCAPLUS Full-text

DOCUMENT NUMBER: 133:9114

TITLE: Methods of making nanocrystalline formulations of human immunodeficiency virus (HIV) protease inhibitors using cellulosic surface stabilizers

INVENTOR(S): Liversidge, Gary G.; Engers, David A.; Roberts, Mary E.; Ruddy, Stephen B.; Wong, Sui-Ming; Xu, Shuqian

PATENT ASSIGNEE(S): Elan Pharma International Limited, Ire.

SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 800,006.
CODEN: USXXAM

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6068858	A	20000530	US 1999-225493	19990106 <--
PRIORITY APPLN. INFO.:			US 1997-800006 A2	19970213

AB The present invention describes formulations of nanoparticulate HIV protease inhibitors comprising a cellulosic surface stabilizer. The nanoparticulate formulations have an increased rate of dissoln. in vitro, an increased rate of absorption in vivo, a decreased fed/fasted ratio variability, and a decreased variability in absorption. The present invention is also directed to methods of making the novel formulations. In particular, nanoparticulate formulations of HIV type 1 (HIV-1) and type 2 (HV-2) protease inhibitors are described. A solution of indinavir was dispensed incrementally into the surface stabilizer solution comprising 2.75 mL 1.0% of super low viscosity hydroxypropyl cellulose in purified water until the entire amount was added. Then, 7.5 mL of 0.5 mm yttria doped zirconia beads was charged into the solution in roller mill bottle, with the roller speed set at 160 rpm and milled for 12 days. Following particle size anal., it was determined that the mean size of the indinavir/hydroxypropyl cellulose nanoparticles was 127 nm.

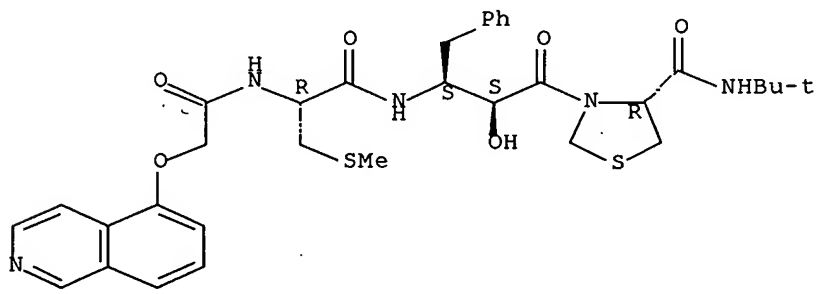
IT **147318-81-8**, KNI-272.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of making nanocryst. formulations of human immunodeficiency virus (HIV) protease **inhibitors** using cellulosic surface stabilizers)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:277960 HCAPLUS Full-text

DOCUMENT NUMBER: 132:308661

TITLE: Preparation of (substituted)acyl dipeptidyl inhibitors of the ice/ced-3 family of cysteine proteases

INVENTOR(S): Karanewsky, Donald S.; Kalish, Vincent J.; Robinson, Edward D.; Ullman, Brett R.

PATENT ASSIGNEE(S): Idun Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023421	A1	20000427	WO 1999-US24756	19991022 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6242422	B1	20010605	US 1998-177546	19981022 <--
CA 2347792	AA	20000427	CA 1999-2347792	19991022 <--
EP 1123272	A1	20010816	EP 1999-970657	19991022 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002527504	T2	20020827	JP 2000-577149	19991022 <--
US 2002091089	A1	20020711	US 2001-836442	20010416 <--

NO 2001001968	A	20010619	NO 2001-1968		20010420 <--
US 2004259804	A1	20041223	US 2001-912674		20010720
PRIORITY APPLN. INFO.:			US 1998-177546	A	19981022
			WO 1999-US24756	W	19991022

OTHER SOURCE(S): MARPAT 132:308661

AB Compds. of formula R1X(CH2)nCHR2CO-A-NHCH[(CH2)qCO2R3]CO-B [A is a natural or unnatural amino acid; B = H, D, alkyl, cycloalkyl, (un)substituted Ph or naphthyl, 2-benzoxazolyl, halomethyl, (CH2)mcycloalkyl, (CH2)m(1- or 2-naphthyl), substituted 2-oxazolyl, (un)substituted (CH2)mphenyl, CH2OCO(aryl), or CH2OCO(heteroaryl), etc.; X = CH2, CO, O, S, NH, CONH, CH2OCONH; R1 = (un)substituted Ph, naphthyl, or heteroaryl; R2 = H, alkyl, cycloalkyl, (un)substituted Ph, (CH2)mNH2, (un)substituted (CH2)mphenyl, (CH2)mcycloalkyl, (CH2)mheteroaryl, etc.; R3 = H, alkyl, cycloalkyl, (cycloalkyl)alkyl, (un)substituted phenylalkyl; m = 1-4, n = 0-2; q = 1-2] or their pharmaceutically acceptable salts were prepared as inhibitors of ICE/ced-3 family of cysteine proteases (ICE = interleukin-1β converting enzyme). Thus, coupling of (1-naphthylamino)acetic acid with (3S)-3-(leucinylamino)-4-oxobutanoic acid tert-Bu ester semicarbazone (preparation given) followed by deprotection of the resulting intermediate with TFA, and treatment with a 3:1:1 solution of MeOH/AcOH/37% HCHO afforded (3S)-3-[[N-((1-naphthylamino)acetyl)leucinyl]amino]-4-oxobutanoic acid which showed IC50 = 0.033 μM for mICE, 0.013 μM for CPP32, and 0.037 μM for MCH-2 enzyme assays, resp. The invention is also directed to pharmaceutical compns. containing these compds., as well as the use of such compns. in the treatment of patients suffering inflammatory, autoimmune and neurodegenerative diseases, for the prevention of ischemic injury, and for the preservation of organs that are to undergo a transplantation procedure.

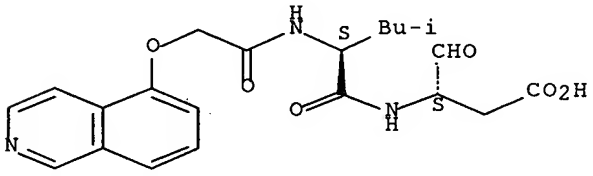
IT **265117-52-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (substituted)acyl dipeptidyl **inhibitors** of the ice/ced-3 family of cysteine proteases)

RN 265117-52-0 HCAPLUS

CN Butanoic acid, 3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-4-methyl-1-oxopentyl]amino]-4-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

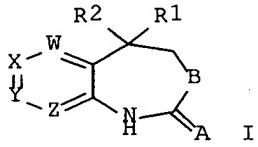
ACCESSION NUMBER:	2000:15187 HCAPLUS Full-text
DOCUMENT NUMBER:	132:78576
TITLE:	1,3-benzodiazepin-2-ones and 1,3-benzoxazepin-2-ones useful as HIV reverse transcriptase inhibitors
INVENTOR(S):	Rodgers, James D.; Cocuzza, Anthony J.
PATENT ASSIGNEE(S):	Du Pont Pharmaceuticals Company, USA
SOURCE:	PCT Int. Appl., 163 pp.

CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000479	A1	20000106	WO 1999-US13872	19990618 <--
W: AU, BR, CA, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IT, LI, LU, MC, PT, SE				
CA 2330110	AA	20000106	CA 1999-2330110	19990618 <--
AU 9946983	A1	20000117	AU 1999-46983	19990618 <--
EP 1091944	A1	20010418	EP 1999-930440	19990618 <--
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2003534230	T2	20031118	JP 2000-557240	19990618

PRIORITY APPLN. INFO.:
US 1998-19252P P 19980630
WO 1999-US13872 W 19990618

OTHER SOURCE(S): MARPAT 132:78576
GI



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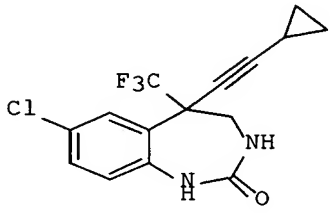


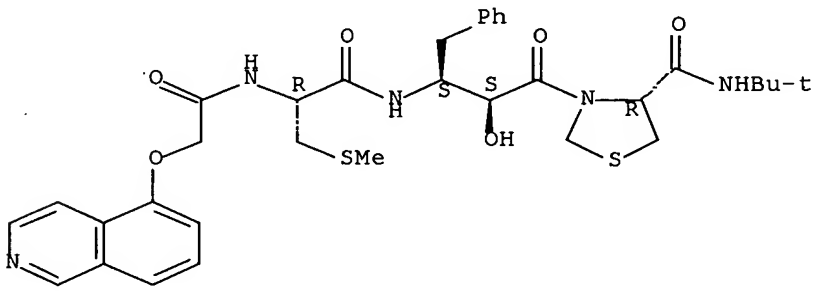
II

AB Title compds. (I) [wherein A = O or S; B = O, S, or (un)substituted amino; W = N or CR3; X = N or CR3A; Y = N or CR3B; Z = N or CR3C; R1 = (halo)alkyl or (cyclopropyl)alkyl; R2 = H, Me, Et, i-Pr, n-Pr, OH, alkoxy, alkenyloxy, alkynyloxy, alkylthio, alkenylthio, alkynylthio, alkylamino, alkenylamino, alkynylamino, 4-7 membered cyclic amine, etc.; R3, R3A, R3B, and R3C = independently H, alkyl, OH, alkoxy, OCF3, halo, NO2, CN, acyl, acylamino, alkylsulfonylamino, phenylsulfonylamino, (un)substituted amino, ureido, or aminosulfonyl, or 5-6 membered heteroarom. ring containing 1-4 O, N, and/or S] were prepared for the treatment of HIV infection. For instance, II was synthesized in a 8-step sequence involving (1) amidation of 4-chloro-2-(trifluoroacetyl)aniline with bromoacetyl bromide, (2) addition of benzenesulfinate, followed by cyclization to form 6-chloro-4-hydroxy-3-(phenylsulfonyl)-1,2,3,4-tetrahydro-4-(trifluoromethyl)quinolin-2-one (89%), (3) reduction to the 2(1H)-quinolinone (93%), (4) 4-addition of cyclopropylacetylene (60%), (5) 3-elimination (90%), (6) N-protection with (BOC)2O (93%), (7) ring opening and amidation with NH2OH.HCl (95%), (8) cyclization and N-deprotection with TsCl/NaOH in dioxane (40%). A number of the compds. of the invention exhibited an IC90 of ≤ 20 μM in an HIV RNA assay using HIV-1 infected MT-2 cells, thereby confirming the utility of the compds. as effective HIV reverse transcriptase inhibitors. The invention compds., their stereoisomeric forms, stereoisomeric mixts., or pharmaceutically acceptable salt forms are useful in pharmaceutical compns. for treating HIV and other viral infections, in diagnostic kits, or as an assay standard or reagent. Claims also include treatment of HIV infection by coadministration

of I with at least one other HIV reverse transcriptase inhibitor and/or HIV protease inhibitor.

IT **147318-81-8**, KNI 272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical coadministration of 1,3-benzodiazepin-2-one or 1,3-benzoxazepin-2-one antivirals with HIV reverse transcriptase **inhibitors** and/or HIV protease **inhibitors** for treatment of HIV infections)
RN 147318-81-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

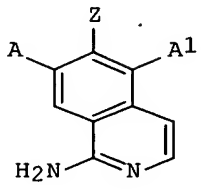
L31 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:613871 HCAPLUS Full-text
DOCUMENT NUMBER: 131:243189
TITLE: Preparation of aminoisoquinoline derivatives as inhibitors of activated blood coagulation factor X
INVENTOR(S): Nakagawa, Tadakiyo; Makino, Shingo; Sagi, Kazuyuki; Takayanagi, Masaru; Kayahara, Takashi; Takehana, Shunji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947503	A1	19990923	WO 1999-JP1309	19990317 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2324153	AA	19990923	CA 1999-2324153	19990317 <--

AU 9928522	A1	19991011	AU 1999-28522	19990317 <--
AU 753675	B2	20021024		
EP 1065200	A1	20010103	EP 1999-909191	19990317 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
US 6825181	B1	20041130	US 2000-665633	20000919
PRIORITY APPLN. INFO.:			JP 1998-70771 A	19980319
			JP 1998-197133 A	19980713
			WO 1999-JP1309 W	19990317

OTHER SOURCE(S): MARPAT 131:243189

GI



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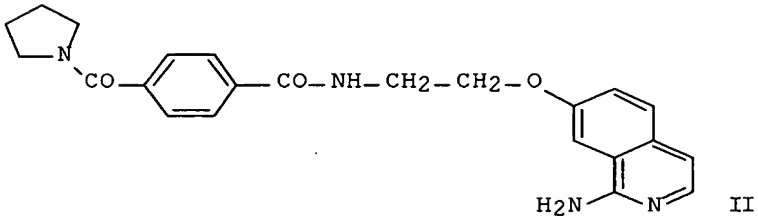


II

AB The title compds. I [A is VLY, A1 is H; or A1 is VLY, A is H ; L is CH2CH2, etc.; V is, for example, H, (un)substituted benzoyl, etc.; extensive details on V are given; Y is CH:CH, etc.; Z = H, alkyl, etc.] are prepared I are useful as active ingredients in anticoagulants or preventives/remedies for thrombosis or embolism. In an in vitro test for inhibition of the activated blood coagulation factor X, the title compound II showed pIC50 of 6.6.

IT **244256-81-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoquinoline derivs. as **inhibitors** of activated blood coagulation factor X)

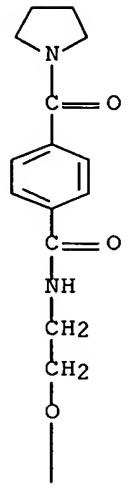
RN 244256-81-3 HCAPLUS

CN Benzamide, N-[2-[(1-amino-5-isoquinolinyl)oxy]ethyl]-4-(1-pyrrolidinylcarbonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

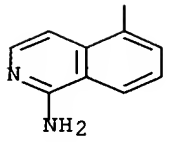
CM 1

CRN 244256-80-2
CMF C23 H24 N4 O3

PAGE 1-A

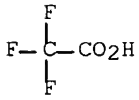


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2

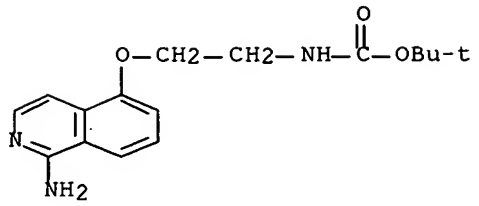


IT **244257-45-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoisoquinoline derivs. as **inhibitors** of activated blood coagulation factor X)
RN 244257-45-2 HCAPLUS
CN Carbamic acid, [2-[(1-amino-5-isoquinolinyl)oxy]ethyl]-, 1,1-dimethylethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

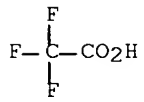
CRN 244257-44-1

CMF C16 H21 N3 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:564981 HCAPLUS Full-text
DOCUMENT NUMBER: 131:196974
TITLE: Preparation of HIV-1 virus mutant for drug resistance study
INVENTOR(S): Ueno, Takamasa
PATENT ASSIGNEE(S): Japan Energy K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 30 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11239486	A2	19990907	JP 1998-300376	19981007 <--
PRIORITY APPLN. INFO.:			US 1997-946021 A	19971007

AB The provirus DNA of a wild type HIV-1 virus in clone pNL4-3 is used to prepare a HIV-1 mutant for use in the study of drug resistance. The mutant exhibits (1) a new SmaI recognition site by substitution mutations at 2591-A→C and 2594-A→G and (2) mutations in the protease region: V32I, M46I, and I84V. The mutations do not jeopardize its infectivity. Use of the mutant NL-V32I/M46I/I84V and other HIV-1 mutants to study the antiviral activity of protease inhibitors such as saquinavir, ritonavir indinavir, and KNI-272 is also shown.

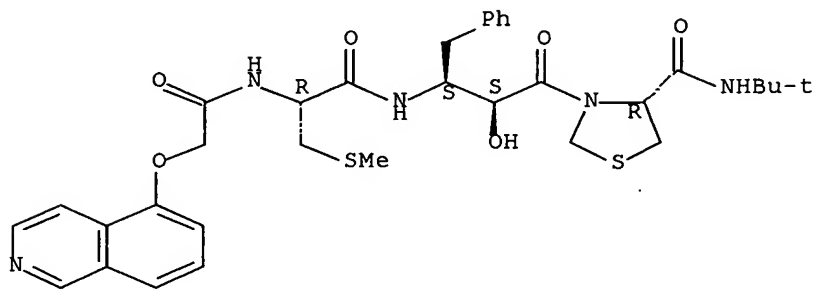
IT **147318-81-8**, KNI-272
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(proteinase **inhibitor**; preparation of HIV-1 virus mutant for drug resistance study)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:487312 HCAPLUS Full-text
DOCUMENT NUMBER: 131:130288
TITLE: Preparation of peptides as efflux pump inhibitors
INVENTOR(S): Chamberland, Suzanne; Lee, May; Lee, Ving J.; Leger, Roger; Renau, Thomas; She, Miles; Zhang, Zhijia J.
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9937667	A1	19990729	WO 1999-US1422		19990122	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
US 6114310	A	20000905	US 1998-12363		19980123	<--
US 6245746	B1	20010612	US 1998-20001		19980204	<--
US 6204279	B1	20010320	US 1998-89734		19980603	<--
AU 9923375	A1	19990809	AU 1999-23375		19990122	<--
US 6436980	B1	20020820	US 2000-724818		20001128	<--
PRIORITY APPLN. INFO.:			US 1998-12363	A	19980123	
			US 1998-20001	A	19980204	
			US 1998-89734	A	19980603	
			WO 1999-US1422	W	19990122	

OTHER SOURCE(S): MARPAT 131:130288

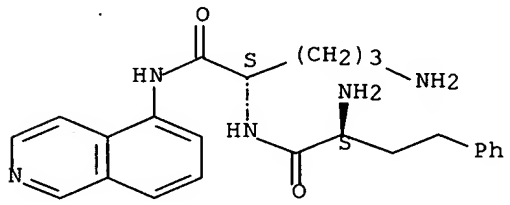
AB Compds. RCHW-A-NR2-CHR1-M-P-X [M = (CH2)n (n = 0, 1, 2), P = CO, CONH, CO2, CH2, CH(OH) of (R)- or (S)-configuration, S, SO, or SO2; A = CO, CH(OH)CH2 of (R)- or (S)-configuration; R, R1, R2 = H, alkyl, fluoroalkyl, mono- or disubstituted aryl, thienyl, furyl, etc.; W = (α-aminoacyl)amido, aminoalkyl, NH2 or mono- or disubstituted amino, (un)substituted heterocyclyl, OH, alkoxy, alkylthio; X = (un)substituted aryl, imidazolyl, oxazolyl, thiazolyl, quinolyl, etc.] were prepared as efflux pump inhibitors which increase the susceptibility of microbes to antimicrobial agents. In vitro microbiol. data for antibiotic potentiation are tabulated for 210 compds., including phenylalanyl- ornithine quinoline-3-amide.

IT **233686-65-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as efflux pump **inhibitors**)

RN 233686-65-2 HCAPLUS

CN Benzenebutanamide, α-amino-N-[(1S)-4-amino-1-[(5-isoquinolinylamino)carbonyl]butyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:404935 HCAPLUS Full-text
DOCUMENT NUMBER: 131:59136
TITLE: Pyridones as Src family SH2 domain inhibitors
INVENTOR(S): Betageri, Rajashekhar; Beaulieu, Pierre L.; Llinas-Brunet, Montse; Ferland, Jean-Marie; Cardozo, Mario; Moss, Neil; Patel, Usha; Proudfoot, John R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931066	A1	19990624	WO 1998-US26123	19981209 <--
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SK, TR, UA, UZ, VN				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2315113	AA	19990624	CA 1998-2315113	19981209 <--
AU 9917194	A1	19990705	AU 1999-17194	19981209 <--
US 6054470	A	20000425	US 1998-208113	19981209 <--

EP 1045836	A1	20001025	EP 1998-962022		19981209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, RO					
JP 2003514762	T2	20030422	JP 2000-538993		19981209
ZA 9811570	A	19990916	ZA 1998-11570		19981217 <--
US 6268365	B1	20010731	US 1999-438629		19991112 <--
US 6284768	B1	20010904	US 1999-438647		19991112 <--
US 6156784	A	20001205	US 1999-455633		19991207 <--
PRIORITY APPLN. INFO.:			US 1997-69971P	P	19971218
			US 1998-208113	A3	19981209
			WO 1998-US26123	W	19981209
			US 1999-129414P	P	19990415

OTHER SOURCE(S): MARPAT 131:59136

AB Compds. A-Q-NB-CH(D-NH-E)-CH2-a-R-C (ring a is selected from cycloalkyl, aryl, heterocyclyl; A = alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, heterocyclyl, aryl; Q = CO, SO2, C:S; B = H, alkyl, a nitrogen-protecting group; R = bond, alkyl, aryl, heterocyclyl, cycloalkyl linker; C is an acidic functionality that carries one or two neg. charges at physiol. pH; D = CH2, CO, C:S; E are certain six-membered unsatd. heterocycles) were prepared These compds. possess the ability to disrupt the interaction between regulatory proteins possessing one or more SH2 domains and their native ligands. Thus, 3-[2'(S)-(1''''- naphthylacetyl)amino-3'-[4''-(1'''-carboxy-1'''-methylethyl)benzene]propanoylamino]-1-(4-methoxybenzyl)-4-methyl-2- pyridone was prepared and showed IC50 = 96 μM for blocking IL-2 production in human blood CD4 pos. T-lymphocytes after T cell receptor and CD28 crosslinking.

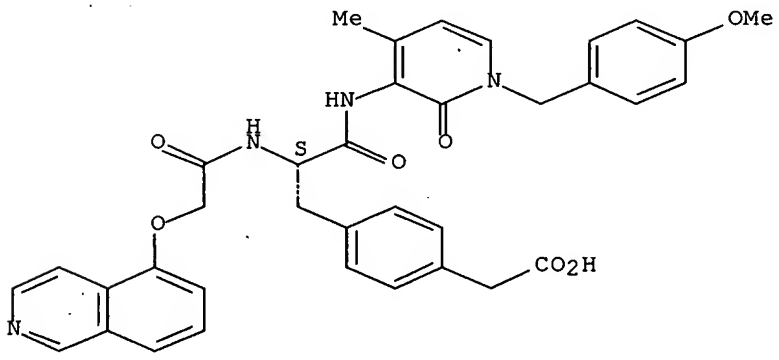
IT **228408-52-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyridones as Src family SH2 domain **inhibitors**)

RN 228408-52-4 HCAPLUS

CN Benzeneacetic acid, 4-[(2S)-3-[[1,2-dihydro-1-[(4-methoxyphenyl)methyl]-4-methyl-2-oxo-3-pyridinyl]amino]-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:282202 HCAPLUS Full-text

DOCUMENT NUMBER: 130:311705

TITLE: Preparation of isoquinolinylguanidines as urokinase

inhibitors.

INVENTOR(S): Barber, Christopher Gordon; Fish, Paul Vincent; Dickinson, Roger Peter

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

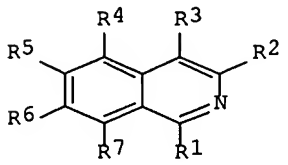
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920608	A1	19990429	WO 1998-EP6353	19981005 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306782	AA	19990429	CA 1998-2306782	19981005 <--
CA 2306782	C	20050517		
AU 9911508	A1	19990510	AU 1999-11508	19981005 <--
AU 727315	B2	20001207		
EP 1023268	A1	20000802	EP 1998-954357	19981005 <--
EP 1023268	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9812922	A	20000808	BR 1998-12922	19981005 <--
TR 200001010	T2	20000921	TR 2000-200001010	19981005 <--
JP 2001520221	T2	20011030	JP 2000-516950	19981005 <--
JP 3600794	B2	20041215		
NZ 503390	A	20020328	NZ 1998-503390	19981005 <--
AT 240943	E	20030615	AT 1998-954357	19981005
PT 1023268	T	20030930	PT 1998-954357	19981005
ES 2197514	T3	20040101	ES 1998-954357	19981005
ZA 9809412	A	20000417	ZA 1998-9412	19981015 <--
AP 959	A	20010417	AP 1998-1366	19981019 <--
W: BW, GM, GH, KE, MW, SD, UG, ZM, ZW				
BG 104328	A	20001229	BG 2000-104328	20000411 <--
NO 2000001924	A	20000615	NO 2000-1924	20000413 <--
HR 2000000217	A1	20001031	HR 2000-217	20000414 <--
US 6248738	B1	20010619	US 2000-424497	20000530 <--

PRIORITY APPLN. INFO.: GB 1997-21964 A 19971016
WO 1998-EP6353 W 19981005

OTHER SOURCE(S): MARPAT 130:311705

GI



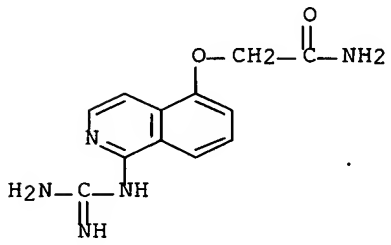
I

AB Title compds. [I; 1 of R1, R2 = H, the other = N:C(NH2)2 or NHC(:NH)NH2; R3 = H, halo, (halo)alkyl, (halo)alkoxy; R4-R7 = H, OH, halo, (substituted) alkyl, alkoxy, alkylcarbonyl, aryl, heteroaryl, cyanoalkoxy, arylsulfonylvinyl, aminocarbonylvinyl, etc.; adjacent pairs of R4-R7 = alkylenedioxy], were prepared Thus, guanidine hydrochloride in Me2SO was stirred with NaH followed by addition of 1-chloroisoquinoline and heating at 100° for 3 days to give 1-isoquinolinylguanidine. Tested I inhibited urokinase with Ki = 63-400 nM.

IT **223670-50-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinolinylguanidines as urokinase **inhibitors**)

RN 223670-50-6 HCAPLUS

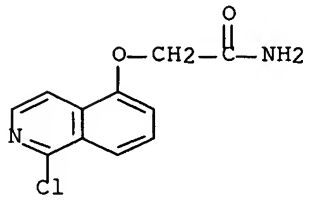
CN Acetamide, 2-[[1-[(aminoiminomethyl)amino]-5-isoquinolinyl]oxy]- (9CI) (CA INDEX NAME)



IT **223671-75-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoquinolinylguanidines as urokinase **inhibitors**)

RN 223671-75-8 HCAPLUS

CN Acetamide, 2-[(1-chloro-5-isoquinolinyl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:509110 HCAPLUS Full-text
DOCUMENT NUMBER: 129:104199
TITLE: Enhanced suppression of HIV-1 by the combination of cytidine nucleoside analogs and CTP synthase inhibitors
INVENTOR(S): Gao, Wen-yi; Johns, David G.; Mitsuya, Hiroaki; Marquez, Victor

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

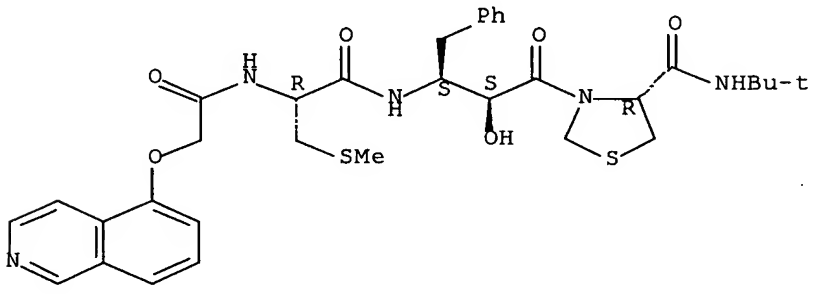
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831375	A1	19980723	WO 1998-US784	19980120 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9858255	A1	19980807	AU 1998-58255	19980120 <--
PRIORITY APPLN. INFO.:			US 1997-33918P	P 19970121
			WO 1998-US784	W 19980120

AB A method is disclosed to increase the potency of cytidine-based anti-HIV drugs using CTP synthase inhibitors, and to overcome resistance of human immunodeficiency virus (HIV) to cytidine-based anti-HIV drugs using CTP synthase inhibitors.

IT **147318-81-8**, KNI272
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV resistant to; cytidine nucleoside analog-CTP synthase **inhibitor** combination for **inhibition** of retrovirus or virus using reverse transcriptase)

RN 147318-81-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 25 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:501276 HCAPLUS Full-text
DOCUMENT NUMBER: 129:170511
TITLE: Use of quinoxalines in three-way combinations with

protease inhibitors and reverse transcriptase inhibitors as a drug for treating AIDS and/or HIV infections

INVENTOR(S): Paessens, Arnold; Blunck, Martin; Riess, Guenter; Kleim, Joerg-Peter; Roesner, Manfred

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX

DOCUMENT TYPE: **Patent**

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19703131	A1	19980730	DE 1997-19703131	19970129 <--
CA 2278773	AA	19980730	CA 1998-2278773	19980115 <--
WO 9832442	A1	19980730	WO 1998-EP197	19980115 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9860940	A1	19980818	AU 1998-60940	19980115 <--
EP 977570	A1	20000209	EP 1998-905297	19980115 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9807523	A	20000321	BR 1998-7523	19980115 <--
JP 2001511124	T2	20010807	JP 1998-531540	19980115 <--
ZA 9800679	A	19980805	ZA 1998-679	19980128 <--
NO 9903670	A	19990910	NO 1999-3670	19990728 <--
MX 9907077	A	20000531	MX 1999-7077	19990729 <--

PRIORITY APPLN. INFO.: DE 1997-19703131 A 19970129
WO 1998-EP197 W 19980115

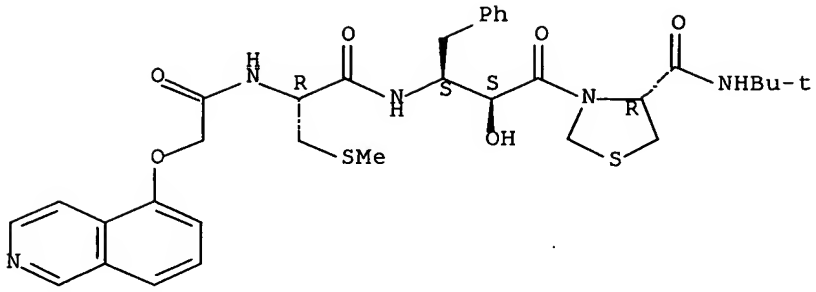
AB Quinoxaline derivs. in combination with protease inhibitors and reverse transcriptase inhibitors inhibited HIV replication in human lymphocytes. Such 3-way combinations are synergistic and may be used to treat persons with HIV infections or AIDS.

IT **147318-81-8**, KNI 272
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AIDS and HIV infections treatment by combinations of quinoxalines and reverse transcriptase **inhibitors** with protease **inhibitors** such as)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 26 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:351758 HCAPLUS Full-text
DOCUMENT NUMBER: 129:45325
TITLE: Liquid pharmaceutical compositions containing HIV protease inhibitors
INVENTOR(S): Lipari, John; Al-Razzak, Laman A.; Ghosh, Soumojeet; Gao, Rong; Kaul, Dilip
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822106	A1	19980528	WO 1997-US20794	19971112 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9710071	A	19980525	ZA 1997-10071	19971107 <--
CA 2271196	AA	19980528	CA 1997-2271196	19971112 <--
AU 9852573	A1	19980610	AU 1998-52573	19971112 <--
AU 717546	B2	20000330		
EP 942721	A1	19990922	EP 1997-947510	19971112 <--
EP 942721	B1	20030122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
CN 1248914	A	20000329	CN 1997-199780	19971112 <--
BR 9714310	A	20000502	BR 1997-14310	19971112 <--
JP 2000515555	T2	20001121	JP 1998-523751	19971112 <--
JP 3592337	B2	20041124		
TR 9901129	T2	20010521	TR 1999-9901129	19971112 <--
NZ 335002	A	20010831	NZ 1997-335002	19971112 <--
EP 1283041	A1	20030212	EP 2002-11533	19971112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
AT 231393	E	20030215	AT 1997-947510	19971112
PT 942721	T	20030630	PT 1997-947510	19971112
IL 129300	A1	20030706	IL 1997-129300	19971112

ES 2191862	T3	20030916	ES 1997-947510	19971112
TW 475895	B	20020211	TW 1997-86117136	19971117 <--
NO 9902427	A	19990720	NO 1999-2427	19990520 <--
KR 2000057169	A	20000915	KR 1999-704469	19990520 <--
BG 64411	B1	20050131	BG 1999-103425	19990521
HK 1022441	A1	20031031	HK 2000-101651	20000317
AU 757970	B2	20030313	AU 2000-39414	20000609
JP 2004346077	A2	20041209	JP 2004-163024	20040601
PRIORITY APPLN. INFO.:			US 1996-754390	A 19961121
			AU 1998-52573	A3 19971112
			EP 1997-947510	A3 19971112
			JP 1998-523751	A3 19971112
			WO 1997-US20794	W 19971112

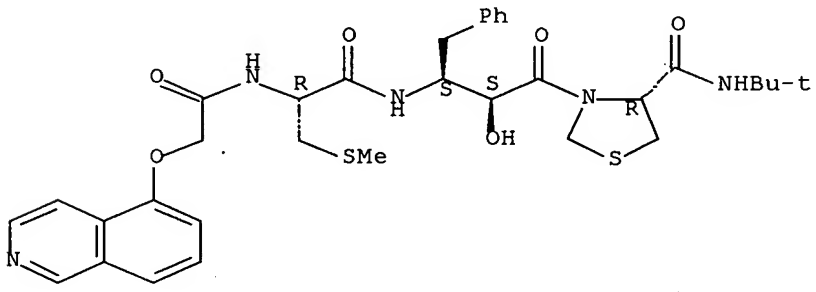
AB A liquid pharmaceutical composition providing improved oral bioavailability is disclosed for compds. which are inhibitors of HIV protease. In particular, the composition comprises a solution in a pharmaceutically acceptable organic solvent of (a) the HIV protease inhibitor and optionally, (b) a surfactant. The composition can optionally be encapsulated in either hard gelating capsules or soft elastic capsules (SEC). A capsule composition was prepared containing ritonavir 20, ethanol 10, oleic acid 69.99, and BHT 0.01% by weight

IT **147318-81-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid pharmaceutical compns. containing HIV protease **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 27 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1998:38687 HCAPLUS Full-text
DOCUMENT NUMBER:	128:154382
TITLE:	Preparation of cis-epoxide compounds as HIV protease inhibitors and anti-AIDS drugs containing them
INVENTOR(S):	Choi, Yo Ken; Choi, Ho Nichi; Park, Shi Hyo; Son, Ei So; Lee, Sho Sen; Yoon, K0 Shok; Kim, Sei Ten; Kou, Kyo En; Kim, Chu Rets
PATENT ASSIGNEE(S):	L. G. Chemical Co., Ltd., S. Korea
SOURCE:	Jpn. Kokai Tokkyo Koho, 17 pp. CODEN: JKXXAF
DOCUMENT TYPE:	**Patent**
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10007672	A2	19980113	JP 1996-168348	19960607 <--
JP 2849810	B2	19990127		

PRIORITY APPLN. INFO.: JP 1996-168348 19960607
OTHER SOURCE(S): MARPAT 128:154382
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

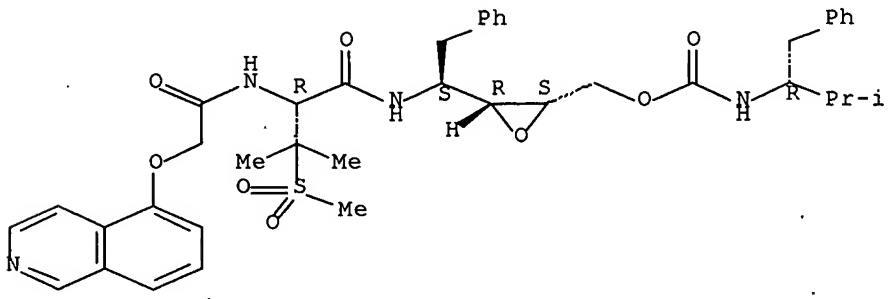
AB The compds. I [R1 = aryl, N-heteroaryl, C1-4 alkyl which may be substituted with aryl or N-heteroaryl, C1-4 alkoxy which may be substituted with aryl or N-heteroaryl; R2 = amino acid residue, C1-4 alkylsulfonyl-C1-8 alkyl; R3 = C1-4 (aryl)alkyl; R4 = H, C1-2 alkyl; R5 = C1-10 (aryl)alkyl; n = 1-2], their salts, hydrates, or solvates are prepared I are prepared by (1) epoxidn. of of II (Cbz = CO2CH2Ph) and coupling of the resulting epoxide with R4R5NH2, (2) deprotection of the resulting III (A = Cbz), (3) coupling of the resulting III (A = H) with IV (R2 = same as in I) or (3') coupling of III (A = H) with IV (R2 = CR62SR7; R6-7 have no definitions) followed by oxidation, (4) deprotection of the resulting V (A = Cbz), (5) coupling of the resulting V (A = H) with R8CO2H (R8 has no definition) or N-acyloxysuccinimides VI. Also claimed are pharmaceutical compns. containing I, their salts, hydrates, or solvates and pharmaceutically acceptable carriers for prevention of HIV infection or for treatment of AIDS. (4S)-[N-(2-benzyloxycarbonyl)-β-methanesulfonyl-L- valinyl]amino-(3R,2S)-epoxy-5-phenyl-1-pentyl N-(2R)-(1-phenyl-3- methylbutyl)carbamate (preparation given) inhibited replication of HIV-1 in H9 cells at IC50 15 μM. CT50 (cytotoxicity) of the compound was >10 μM.

IT **200358-17-4P 200358-18-5P 200358-19-6P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cis-epoxyalkyl carbamates as HIV protease **inhibitors** and anti-AIDS drugs)

RN 200358-17-4 HCAPLUS

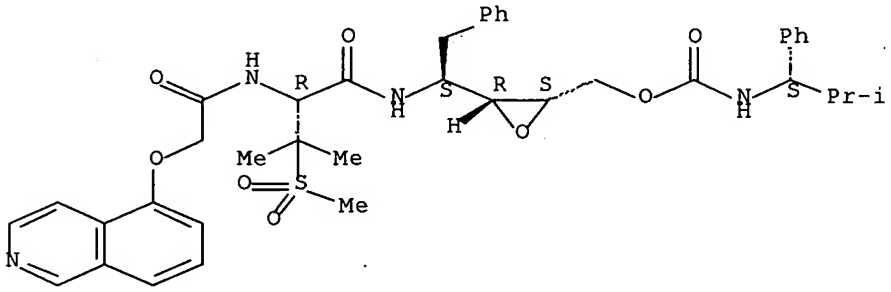
CN L-Arabinitol, 3,4-anhydro-1,2-dideoxy-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl-, 5-[[(1R)-2-methyl-1-(phenylmethyl)propyl]carbamate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



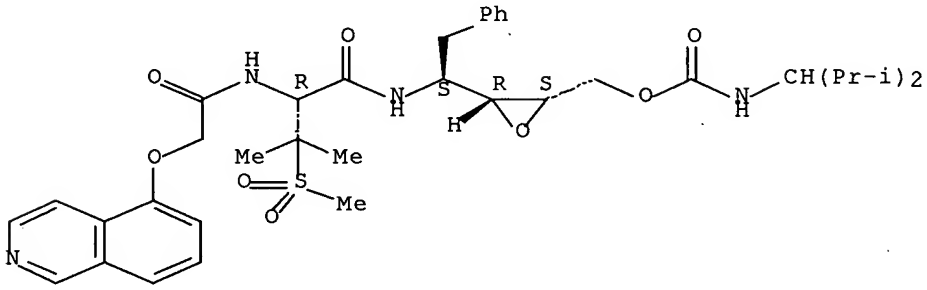
RN 200358-18-5 HCAPLUS
CN L-Arabinitol, 3,4-anhydro-1,2-dideoxy-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl-, 5-[[(1S)-2-methyl-1-phenylpropyl]carbamate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 200358-19-6 HCAPLUS
CN L-Arabinitol, 3,4-anhydro-1,2-dideoxy-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl-, 5-[[2-methyl-1-(1-methylethyl)propyl]carbamate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

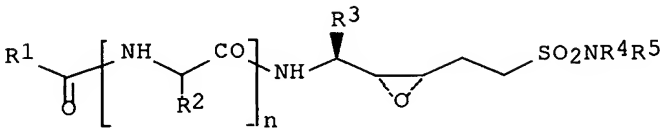


L31 ANSWER 28 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:38656 HCAPLUS Full-text
DOCUMENT NUMBER: 128:149571
TITLE: Preparation of cis-epoxide compounds as HIV protease inhibitors and anti-AIDS drugs containing them
INVENTOR(S): Choi, Nakun; Choi, Ho Il; Park, Chi Hio; Sohn, Yong Chang; Lee, Chang Soon; Yohn, Hyun Sik; Kim, Sun Chung; Koh, Jong Sun; Kim, Chun Ryul
PATENT ASSIGNEE(S): L. G. Chemical Co., Ltd., S. Korea
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 10007554	A2	19980113	JP 1996-145585	19960607 <--
JP 2960350	B2	19991006		
PRIORITY APPLN. INFO.:			JP 1996-145585	19960607
OTHER SOURCE(S):	MARPAT 128:149571			

GI



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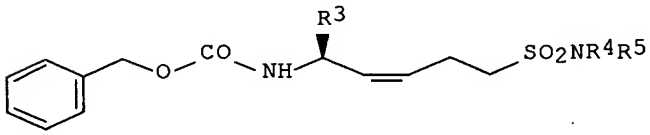
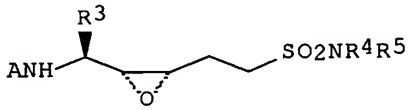
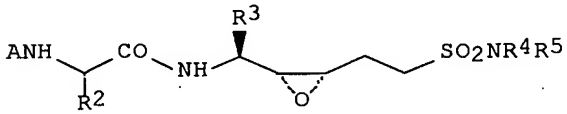


II



III



IV

AB The compds. I (R1 = aryl, N-containing heteroaryl, C1-4 alkyl which may be substituted with aryl, N-containing heteroaryl, C1-4 alkoxy which may be substituted with aryl, N-containing heteroaryl; R2 = amino acid residue, C1-4 alkylsulfonyl-C1-8 alkyl; R3 = C1-4 alkyl which may be substituted with aryl; R4 = H, C1-4 alkyl; R5 = aryl, C1-10 alkyl, aryl-C1-4 alkyl; n = 1-2), their salts, their hydrates, and their solvates are prepared by (1) epoxidn. of II with m-ClC6H4CO3H, (2) deprotection of the resulting III (A = CO2CH2Ph), (3) coupling of the resulting III (A = H) with PhCH2OCONHCH(CR62SR7)CO2H (R6-7 = C1-4 alkyl) followed by oxidation, (4) deprotection of the resulting IV, (5) coupling of the resulting IV (A = = CO2CH2Ph), and (6) coupling of the resulting IV (A = H) with R1CO2H. I are also prepared by directly coupling of III (A = H) with R1CONHCH(R2)CO2H. Also claimed are HIV infection preventive agents and therapeutics for AIDS containing I, their salts, hydrates, or solvates and pharmaceutically acceptable carriers. N-tert-butyl-5-L-(N-benzyloxycarbonyl)amino-6-phenyl- (4R,3S)-epoxyhexanesulfonamide (preparation given) was deprotected upon hydrogenation, and the resulting amine was coupled with N-benzyloxycarbonyl-β-(S-methyl)-L-valine then treated with m-ClC6H4CO3H to give N-tert-butyl-5S-[N-benzyloxycarbonyl-β- methanesulfonyl-L-valinyl]amino-(4R,3S)-epoxy-6-phenylhexanesulfonamide. This compound inhibited replication of HIV-1 in H9 cell at IC50 25 nM. Cytotoxicity of this compound on H9 cell was >10 μL.

IT **198129-67-8P**

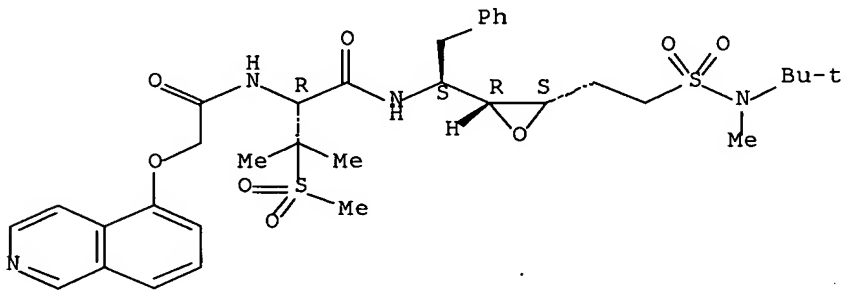
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of cis-epoxyhexanesulfonamides as HIV protease **inhibitors** and anti-AIDS drugs)

RN 198129-67-8 HCAPLUS

CN L-arabino-Hexitol, 3,4-anhydro-1,2,5,6-tetradeoxy-6-[[(1,1-dimethylethyl)methylamino]sulfonyl]-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 29 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:17976 HCAPLUS Full-text

DOCUMENT NUMBER: 128:61798

TITLE: Preparation of epoxide peptidomimetics as irreversible HIV protease inhibitors

INVENTOR(S): Yoon, Heungsik; Choy, Nakyen; Kim, Sung Chun; Choi, Ho Il; Son, Young Chan; Park, Chi Hyo; Moon, Kwang-yul; Jung, Wonhee; Kim, Chung Ryeol; Lee, Chang Sun; Koh, Jong Sung; Kim, Sang Soo

PATENT ASSIGNEE(S): LG Chemical Ltd., S. Korea

SOURCE: U.S., 50 pp., Cont.-in-part of U.S. Ser. No. 341,352, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 5696134	A	19971209	US 1995-473877	19950607	<--
US 5587388	A	19961224	US 1993-159382	19931130	<--
KR 125117	B1	19971205	KR 1994-13423	19940615	<--
US 5773468	A	19980630	US 1995-572402	19951214	<--
US 5744621	A	19980428	US 1996-667888	19960620	<--
US 5763631	A	19980609	US 1996-667133	19960620	<--

PRIORITY APPLN. INFO.:

US 1993-159382	A2	19931130
KR 1994-13423	A	19940615
US 1994-341352	B2	19941117
KR 1992-23088	A	19921202
KR 1992-23089	A	19921202
KR 1993-10811	A	19930614
KR 1993-21298	A	19931014
KR 1993-21299	A	19931014
KR 1993-21300	A	19931014
US 1995-473877	A2	19950607

KR 1995-37292 A 19951026

OTHER SOURCE(S): MARPAT 128:61798

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

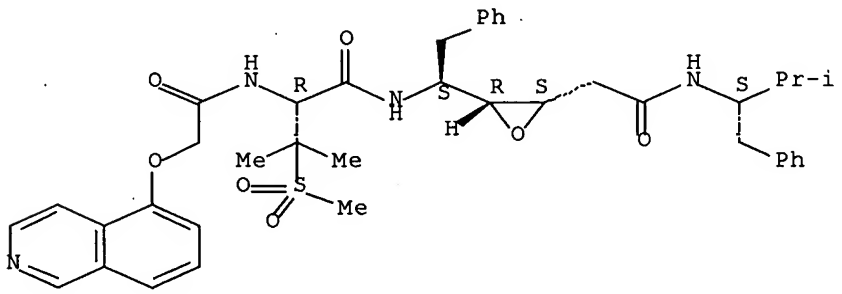
AB Novel cis-epoxide compds. I [R1, R2 = independently H, alkyl; R3 = aryl or alkyl (un)substituted with aromatic, C3-8 cycloalkyl; R4 = H, C1-4 alkyl; n = 0-2; X = CO, COCO, S(O), SO2, CS; Y = O, CH2, NH, NMe; m = 0, 1; R5 = heterocycle; straight, branched, or cyclic C1-8 alkyl; alkyl substituted with heterocycle or cycloalkyl; straight, branched, or cyclic C1-8 alkoxy; aryl-substituted alkoxy; NR6R7; R6 = straight or branched C1-8 alkyl, cycloalkyl, alkyl substituted with cycloalkyl; R7 = H, alkyl; Z = O, NH, NMe; R8, R9 = independently alkyl (un)substituted with aromatic hydrocarbon or cycloalkyl; C3-8 cycloalkyl; aromatic] are useful for treating or preventing diseases caused by HIV infection. The novel HIV protease inhibitors I have specific structures to form stable bonding with the enzyme active site, which entails a highly enhanced irreversible inhibition against HIV protease. Thus deprotection and peptide coupling of olefin II (prepared in 4 steps from protected L-phenylalaninal and (S)-2-amino-3-methyl-1-phenylbutane) with penicillamine-derived sulfone III (prepared in 3 steps from L-penicillamine), followed by epoxidn. with mCPBA gave title epoxide derivative IV. IV showed irreversible inactivation of HIV-1 protease, with a stoichiometric ratio of inhibitor to enzyme of 1:1. IV also showed antiviral activity against HIV-1 with IC50 = 1 nM.

IT **174562-56-2P 174562-57-3P 174562-58-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epoxide peptidomimetics as irreversible HIV protease **inhibitors**)

RN 174562-56-2 HCAPLUS

CN Oxiraneacetamide, 3-[1-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-2-phenylethyl]-N-[2-methyl-1-(phenylmethyl)propyl]-, [2S-[2α(R*),3α[R*(S*)]]]- (9CI) (CA INDEX NAME)

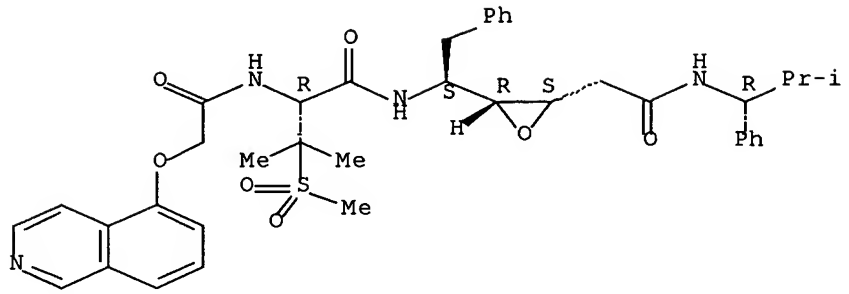
Absolute stereochemistry.



RN 174562-57-3 HCAPLUS

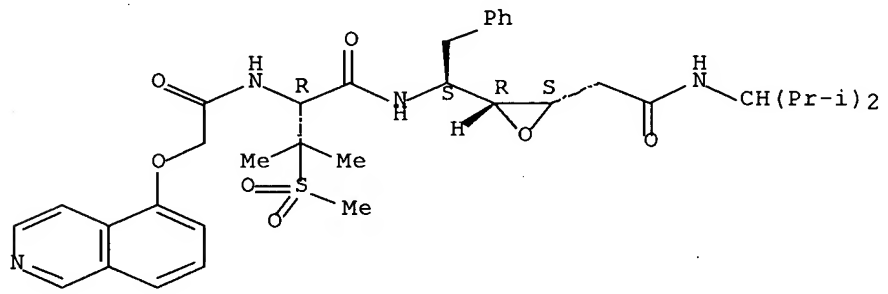
CN Oxiraneacetamide, 3-[1-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-2-phenylethyl]-N-(2-methyl-1-phenylpropyl)-, [2S-[2α(S*),3α[R*(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174562-58-4 HCAPLUS
CN Oxiraneacetamide, 3-[1-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-2-phenylethyl]-N-[2-methyl-1-(1-methylethyl)propyl]-, [2S-[2α,3α[R*(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

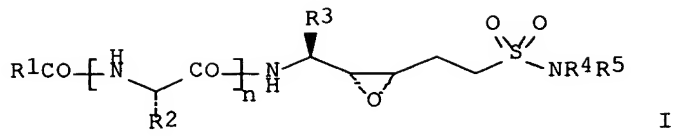


L31 ANSWER 30 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:13700 HCAPLUS Full-text
DOCUMENT NUMBER: 128:75675
TITLE: Preparation of peptidyl cis-epoxides as irreversible HIV protease inhibitors
INVENTOR(S): Choy, Nakyen; Choi, Hoil; Park, Chi-hyo; Son, Young-chan; Lee, Chang-sun; Yoon, Heung-sik; Kim, Sung-chun; Koh, Jong-sung; Kim, Chung-ryeol
PATENT ASSIGNEE(S): Lg Chemical Limited, S. Korea
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 812857	A1	19971217	EP 1996-109336	19960611 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			EP 1996-109336	19960611

OTHER SOURCE(S): MARPAT 128:75675

GI



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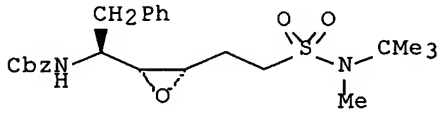


II

AB Title compds. I [R1 = (N-containing) aromatic, (aromatic-substituted) C1-4 alkyl, (aromatic-substituted) C1-4 alkoxy, etc.; R2 = amino acid side chain, (C1-4 alkylsulfonyl-substituted) C1-8 alkyl; R3 = (aromatic-substituted) C1-4 alkyl; R4 = H, C1-4 alkyl; R5 = aromatic group, C1-10 alkyl, (aromatic-substituted) C1-4 alkyl; n = 1,2] were prepared For example, the synthesis of the title compds. included the stepwise synthesis of intermediates such as II from such starting materials as MeNHCMe3, Cl(CH2)3SO2Cl, and (S)-CbzNHCH(CH2Ph)CHO. Cis-epoxide I (R1 = PhCH2O; R2 = C(Me)2SO2Me; R3 = CH2Ph; R4 = Me; R5 = CMe3; n = 1) was obtained at 75% yield by the coupling of Cbz-deprotected intermediate II and N-benzyloxycarbonyl-β-(S-methyl)-L-valine in presence of EDC and HOBT in DMF, followed by oxidation of the thio moiety by m-chloroperoxybenzoic acid. In an assay for the inhibition of HIV protease, IC50 value of the above cis-epoxide I was 1 nM vs. 12 nM of AZT (azidothymidine) and 7 nM of Ro-31-8959. The cytotoxicities (CT50) of the title compds. were measured and found to be equivalent to those of AZT and Ro-31-8959.

IT **198129-67-8P**

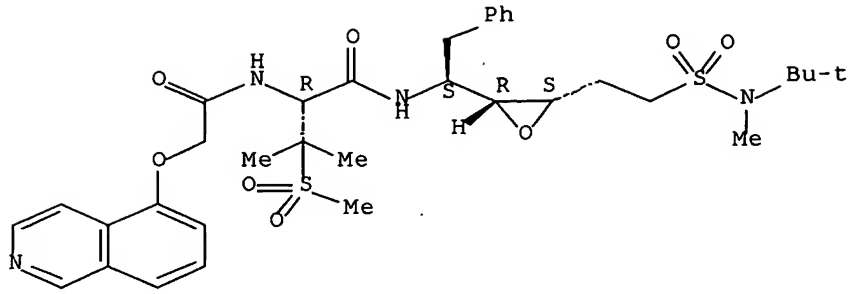
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptidyl cis-epoxides as irreversible HIV protease **inhibitors**)

RN 198129-67-8 HCAPLUS

CN L-arabino-Hexitol, 3,4-anhydro-1,2,5,6-tetradeoxy-6-[[(1,1-dimethylethyl)methylamino]sulfonyl]-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl- (9CI) (CA INDEX NAME)

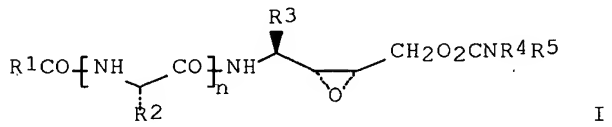
Absolute stereochemistry.



L31 ANSWER 31 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:13690 HCAPLUS Full-text
DOCUMENT NUMBER: 128:61796
TITLE: Preparation of irreversible HIV protease inhibitors and compositions containing the same
INVENTOR(S): Choy, Nakyen; Choi, Hoil; Park, Chi-hyo; Son, Young-chan; Lee, Chang-sun; Yoon, Heung-sik; Kim, Sung-chun; Koh, Jong-sung; Kim, Chung-ryeol
PATENT ASSIGNEE(S): Lg Chemical Limited, S. Korea
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 812839	A1	19971217	EP 1996-109335	19960611 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			EP 1996-109335	19960611

OTHER SOURCE(S): MARPAT 128:61796
GI



I

AB Cis-epoxide compds. I (R1 = aromatic or nitrogen-containing aromatic group, alkyl or alkoxy optionally substituted with aromatic or nitrogen-containing aromatic group; R2 = amino acid residue, alkylsulfonylalkyl; R3, R5 = alkyl, arylalkyl; R4 = H, alkyl; n = 1 or 2) were prepared as HIV protease inhibitors. Thus, 4S-[[N-(2-quinolinecarbonyl)-L-asparaginyl]amino]-(3R,2S)-epoxy-5- phenylpentyl N-1R-(1-benzyl-2-methylpropyl)carbamate was prepared and assayed for antiviral activity (IC50 = 125 nM) and cytotoxicity (CT50 = >10 μM).

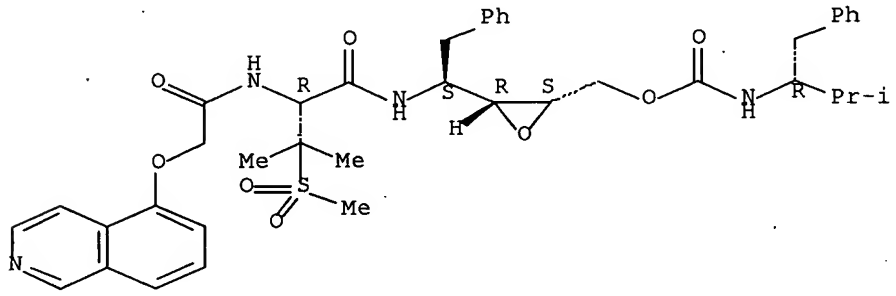
IT **200358-17-4P 200358-18-5P 200358-19-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of irreversible HIV protease **inhibitors**)

RN 200358-17-4 HCAPLUS

CN L-Arabinitol, 3,4-anhydro-1,2-dideoxy-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl-, 5-[[(1R)-2-methyl-1-(phenylmethyl)propyl]carbamate] (9CI) (CA INDEX NAME)

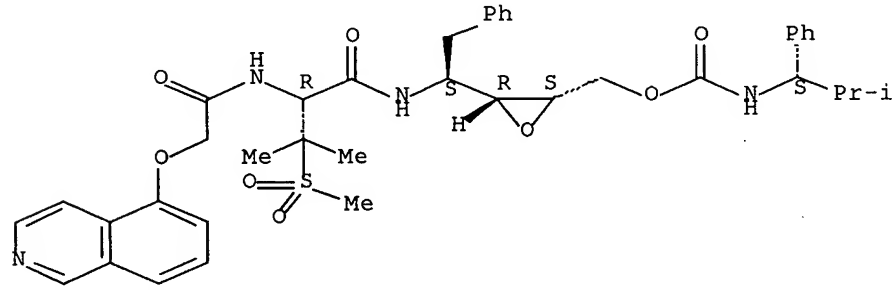
Absolute stereochemistry.



RN 200358-18-5 HCAPLUS

CN L-Arabinitol, 3,4-anhydro-1,2-dideoxy-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl-, 5-[[(1S)-2-methyl-1-phenylpropyl]carbamate] (9CI) (CA INDEX NAME)

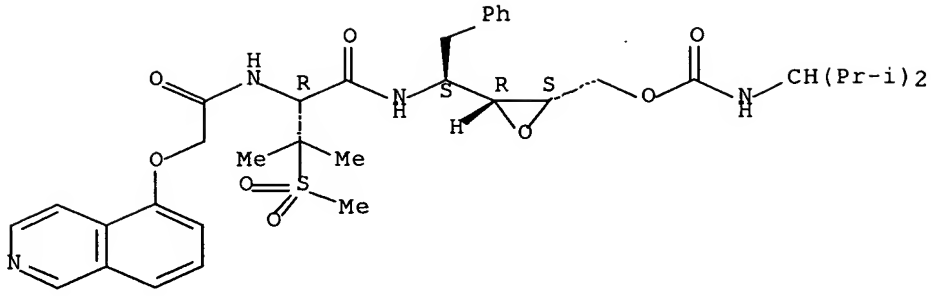
Absolute stereochemistry.



RN 200358-19-6 HCAPLUS

CN L-Arabinitol, 3,4-anhydro-1,2-dideoxy-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl-, 5-[[2-methyl-1-(1-methylethyl)propyl]carbamate] (9CI) (CA INDEX NAME)

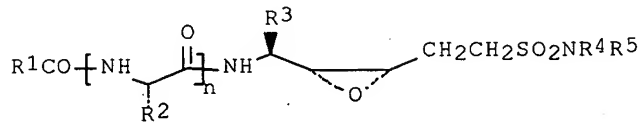
Absolute stereochemistry.



L31 ANSWER 32 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:735760 HCAPLUS Full-text
DOCUMENT NUMBER: 127:346662
TITLE: Preparation of irreversible HIV protease inhibitors
INVENTOR(S): Choy, Nakyen; Choi, Hoil; Park, Chi Hyo; Son, Young Chan; Lee, Chang Sun; Yoon, Heungsik; Kim, Sung Chun; Koh, Jong Sung; Kim, Chung Ryeol
PATENT ASSIGNEE(S): LG Chemical Ltd., S. Korea
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 341,352.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5679687	A	19971021	US 1996-659794	19960606 <--
US 5587388	A	19961224	US 1993-159382	19931130 <--
KR 154912	B1	19981201	KR 1994-33270	19941208 <--
US 5744621	A	19980428	US 1996-667888	19960620 <--
US 5763631	A	19980609	US 1996-667133	19960620 <--
PRIORITY APPLN. INFO.:			US 1993-159382	A2 19931130
			US 1994-341352	A2 19941117
			KR 1994-33270	A 19941208
			KR 1992-23088	A 19921202
			KR 1992-23089	A 19921202
			KR 1993-10811	A 19930614
			KR 1993-21298	A 19931014
			KR 1993-21299	A 19931014
			KR 1993-21300	A 19931014

OTHER SOURCE(S): MARPAT 127:346662
GI



I

AB Cis-epoxide compds. I (R1 = aromatic group, nitrogen-containing aromatic group, alkyl or alkoxy optionally substituted by aromatic or nitrogen-containing aromatic group; R2 = amino acid residue, alkylsulfonylalkyl; R3 =

alkyl, arylalkyl; R4 = H, alkyl; R5 = aryl, alkyl, arylalkyl; n = 1, 2) were prepared as inhibitors of human immunodeficiency virus (HIV) protease. Thus, N-tert-butyl-5S-[[N-(benzyloxycarbonyl)-β-methanesulfonyl-L- valinyl]amino]-(4R,3S)-epoxy-6-phenylhexanesulfonamide was prepared and assayed for antiviral activity (IC50 = 25 nM) and cytotoxicity (CT50 = >10 μM).

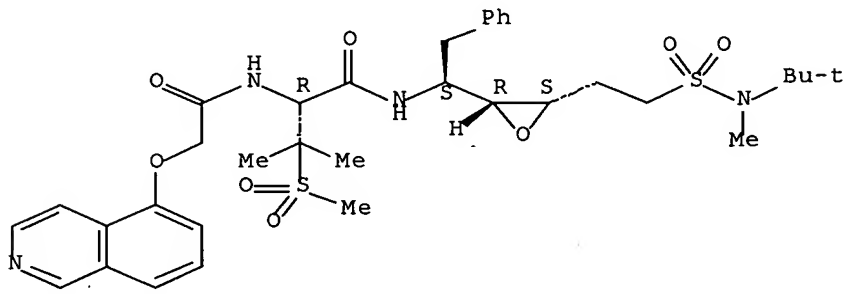
IT **198129-67-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of irreversible HIV protease **inhibitors**)

RN 198129-67-8 HCAPLUS

CN L-arabino-Hexitol, 3,4-anhydro-1,2,5,6-tetradeoxy-6-[[(1,1-dimethylethyl)methylamino]sulfonyl]-2-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 33 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:276427 HCAPLUS Full-text

DOCUMENT NUMBER: 126:246812

TITLE: Enhancement of the biological and antiviral activity of HIV protease inhibitors with macrolide and lincosamide antibiotics

INVENTOR(S): Schinazi, Raymond F.; Sommadossi, Jean-Pierre

PATENT ASSIGNEE(S): University of Alabama at Birmingham, USA; Schinazi, Raymond, F.

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708180	A1	19970306	WO 1996-US13721	19960830 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5750493	A	19980512	US 1995-521474	19950830 <--
AU 9668601	A1	19970319	AU 1996-68601	19960830 <--

AU 716821 B2 20000309
EP 876387 A1 19981111 EP 1996-929058 19960830 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2001500471 T2 20010116 JP 1997-510502 19960830 <--
PRIORITY APPLN. INFO.: US 1995-521474 A 19950830
WO 1996-US13721 W 19960830

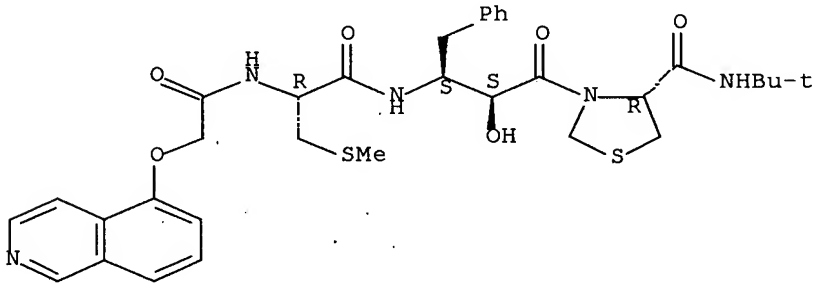
AB The cellular uptake of protease inhibitors (e.g. HIV protease inhibitor), in antiviral therapy based on inhibition of a protease required for viral maturation, is diminished by binding of the protease inhibitor to α1-acid glycoprotein (AAG), an acute-phase protein in serum. This effect is reversed, and the antiviral effectiveness of the protease inhibitors is restored, by coadministration of ≥1 AAG-binding compound, such as a macrolide or lincosamide antibiotic, which has sufficient binding affinity for AAG to competitively bind AAG in the presence of the protease inhibitor. Thus, cellular accumulation of HIV protease inhibitor SC-52151 by phytohemagglutinin-stimulated human peripheral blood mononuclear cells in the presence of AAG (1 mg/mL) was completely restored (to the level observed in the absence of AAG) by addition of erythromycin to 500 μM.

IT **147318-81-8**, KNI 272
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of biol. and antiviral activity of HIV protease **inhibitors** with macrolide and lincosamide antibiotics)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 34 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:204402 HCAPLUS Full-text
DOCUMENT NUMBER: 126:277256
TITLE: Preparation of hydrazides as inhibitors of metazoan parasite proteases
INVENTOR(S): Cohen, Fred E.; Mckerrow, James H.; Ring, Christine S.; Rosenthal, Philip J.; Kenyon, George L.; Li, Zhe
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: U.S., 23 pp., Cont.-in-part of U. S. Ser. No. 943,925, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

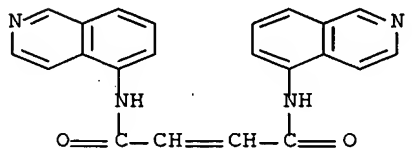
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5610192	A	19970311	US 1995-387760	19950328 <--
WO 9406280	A1	19940331	WO 1993-US8708	19930913 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5739170	A	19980414	US 1995-413337	19950330 <--
US 6194421	B1	20010227	US 1997-801	19971230 <--
US 6548521	B1	20030415	US 2000-628080	20000728
PRIORITY APPLN. INFO.:			US 1992-943925 B2	19920911
			WO 1993-US8708 W	19930913
			US 1995-387760 A2	19950328
			US 1995-413337 A1	19950330
			US 1997-801 A1	19971230

OTHER SOURCE(S): MARPAT 126:277256

AB Metazoan parasite protease inhibitors AXB [A = substituted or unsubstituted homoarom. ring, e.g. Ph, 1-naphthyl, 1-isoquinolyl, 1-phthalazinyl, 3-coumarinyl, 9-phenanthryl, 1-quinolyl; B = substituted or unsubstituted homoarom. ring comprising 1-3 rings, e.g., Ph, 1-naphthyl, 2-naphthyl, 1-isoquinolyl, 1-phthalazinyl, 3-coumarinyl, 9-phenanthryl, 1-quinolyl, 2-quinolyl, 6-coumarinyl, 2-chromonyl; X = a linker 4-8 atoms in length, e.g, CR:NN:CR (R = H, alkyl), NRCOCONR (R = H, alkyl), CR:NNR'C(:Y) (R = H, alkyl; R' = H, alkyl, aryl; Y = O, S), etc.] were prepared E.g., condensation of salicylic aldehyde and oxalic dihydrazide gave 97% oxalic bis(2-hydroxy-1-phenylmethylene)hydrazide (I). In a trophozoite cysteine protease inhibition study, IC50 for I was >60μm. The compns. comprise at least one metazoan protease inhibitor which binds to the S2 subsite and at least one of the S1 and S1' subsites of the metazoan parasite protease.

IT **155062-60-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of hydrazides as **inhibitors** of metazoan parasite proteases)

RN 155062-60-5 HCAPLUS
CN 2-Butenediamide, N,N'-di-5-isoquinolinyl- (9CI) (CA INDEX NAME)



L31 ANSWER 35 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:184660 HCAPLUS Full-text
DOCUMENT NUMBER: 126:166463
TITLE: Use of ritonavir (ABT-538) for improving the pharmacokinetics of drugs metabolized by cytochrome P450 in a method of treating aids
INVENTOR(S): Norbeck, Daniel W.; Kempf, Dale J.; Leonard, John M.;

Bertz, Richard J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9701349	A1	19970116	WO 1996-US11015	19960628 <--
W: AU, CA, IS, JP, KR, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6037157	A	20000314	US 1996-687774	19960626 <--
CA 2224738	AA	19970116	CA 1996-2224738	19960628 <--
CA 2224738	C	20020827		
AU 9663420	A1	19970130	AU 1996-63420	19960628 <--
AU 722812	B2	20000810		
EP 871465	A1	19981021	EP 1996-922604	19960628 <--
EP 871465	B1	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11508884	T2	19990803	JP 1997-504572	19960628 <--
EP 1210941	A2	20020605	EP 2001-204308	19960628 <--
EP 1210941	A3	20020731		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 225186	E	20021015	AT 1996-922604	19960628 <--
EP 1273298	A2	20030108	EP 2002-79002	19960628
EP 1273298	A3	20030319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
EP 1284140	A2	20030219	EP 2002-79003	19960628
EP 1284140	A3	20030319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
EP 1293207	A1	20030319	EP 2002-79004	19960628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
ES 2186787	T3	20030516	ES 1996-922604	19960628
HK 1016088	A1	20030808	HK 1999-101376	19990407
AU 759386	B2	20030410	AU 2000-56443	20000904
US 2002039998	A1	20020404	US 2001-957171	20010920 <--
US 6703403	B2	20040309		

PRIORITY APPLN. INFO.:		
US 1995-654P	P	19950629
US 1995-3849P	P	19950915
US 1996-687774	A3	19960626
AU 1996-63420	A3	19960628
EP 1996-922604	A3	19960628
WO 1996-US11015	W	19960628
US 1999-387261	A3	19990831

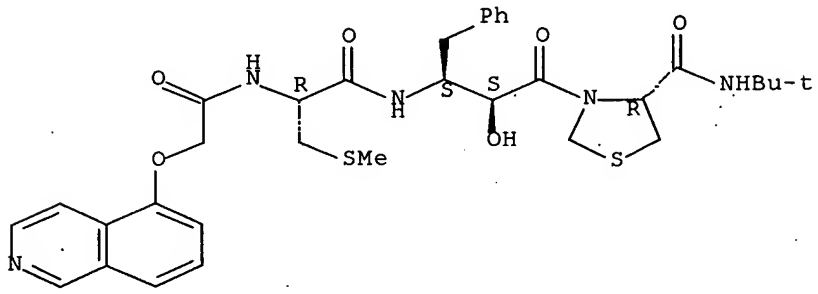
AB A method is disclosed for improving the pharmacokinetics of a drug which is metabolized by cytochrome P 450 monooxygenase by use of ritonavir. HIV inhibitory action is also claimed by combinations of ritonavir with protease inhibitors whose pharmacokinetics are modulated by ritanovir via its inhibitory action on cytochrome P 450.

IT **147318-81-8**, Kni 272
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ritonavir **inhibits** P 450 and modulates drug pharmacokinetics and combined HIV antiviral action with protease **inhibitors**)

RN 147318-81-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-

[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

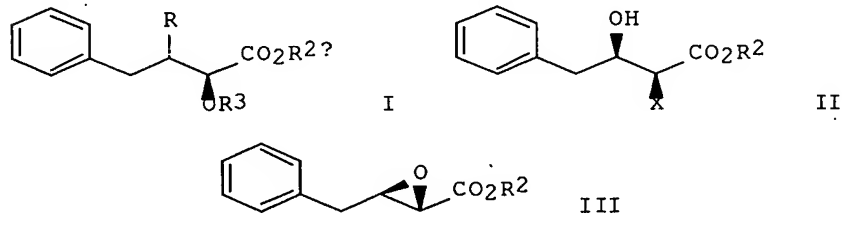
Absolute stereochemistry.



L31 ANSWER 36 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:641285 HCAPLUS Full-text
DOCUMENT NUMBER: 125:276572
TITLE: Process for preparing optically active allophenylnorstatin derivatives via asymmetric hydrogenation of 4-phenyl-2-halo-3-oxobutyric ester
INVENTOR(S): Sayo, Noboru; Yamasaki, Tetsuro; Kumobayashi, Hidenori; Yuasa, Yoshifumi; Sotoguchi, Tsukasa
PATENT ASSIGNEE(S): Takasago International Corporation, Japan
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729939	A2	19960904	EP 1996-301421	19960301 <--
EP 729939	A3	19970917		
R: BE, CH, DE, FR, GB, IT, LI, NL				
JP 08231482	A2	19960910	JP 1995-41791	19950301 <--
US 5581007	A	19961203	US 1996-609619	19960301 <--
PRIORITY APPLN. INFO.:			JP 1995-41791 A	19950301

OTHER SOURCE(S): CASREACT 125:276572; MARPAT 125:276572
GI



AB A process for preparing an optically active (2S,3S)-allophenylnorstatin derivative [I; R = protected NH2; R2a = H, lower alkyl; R3 = H, tri(lower alkyl) silyl, (lower alkyl)diarylsilyl] comprises asym. hydrogenating a 4-phenyl-2-halo-3-oxobutyric ester PhCH2COCHXCO2R2 (R2 = lower alkyl; X = halo) in the presence of a ruthenium-phosphine complex to obtain a 4-phenyl-(2S)-halo-(3R)-hydroxybutyric ester (II; R2, X = same as above), epoxidizing the latter ester in the presence of a base to obtain a 4-phenyl-(2S,3R)-epoxybutyric ester (III; R2 = same as above), reacting the latter ester with a tri(lower alkyl)silyl azide or a (lower alkyl)diarylsilyl azide in the presence of a Lewis Acid to obtain a (3S)-azido-4-phenyl-(2S)-trisubstituted silyloxybutyric ester I [R = N3; R2a = lower alkyl; R3 = tri(lower alkyl) silyl, (lower alkyl)diarylsilyl], hydrogenolyzing the latter ester into a (2S,3S)-allophenylnorstatin derivative I [R = NH2; R2a = lower alkyl; R3 = tri(lower alkyl) silyl, (lower alkyl)diarylsilyl], protecting the amino group of the latter compound, and, if desired, hydrolyzing the compound before or after the amino group protection. The desired compds., useful as intermediates for HIV protease inhibitor, can be safely obtained at high optical purity and in good yield. Thus, 50 g PhCH2COCHClCO2Me, 99.4 mg Ru2Cl4[(R)-T-BINAP]2NEt3, and 100 mL isopropanol were placed in a Hastelloy autoclave under N, heated, pressurized with H at 30 atm, and hydrogenated at 100° for 1-2 h to give a 87:13 ratio of syn-isomer II (X = Cl, R2 = Me) (80.5 %e.e.) and anti-isomer (94.6 %e.e.), resp., in a yield of 98.6%. A solution of 57.2 g II (X = Cl, R2 = Me) in MeOH was added dropwise to a mixture of 59.4 g 28% NaOMe in MeOH and 60 mL MeOH under ice-cooling and stirred at the same temperature for 2 h to give, after workup, 75% III (R2 = Me). The latter compound (31.5 g) was stirred with 23.1 g Me3SiN3 at 70° for 20 h to give 79.1% I (R = N3, R2a = Me, R3 = Me3Si). The latter compound (41.7 g) was hydrogenated in the presence of 5% Pd-C in THF at 50° and 20 atm H pressure for 20 h in an autoclave, filtered through Celite, and after evaporating the solvent, the residue was cooled in an ice bath, treated with 200 mL 1 N aqueous NaOH, stirred at room temperature for overnight, treated dropwise with 32.6 g di-tert-Bu dicarbonate and 135 mL THF in an ice bath, and stirred at room temperature overnight to give, after workup and acidification with 20% aqueous H3PO4, 85% I (R = BocNH, R2a = R3 = H).

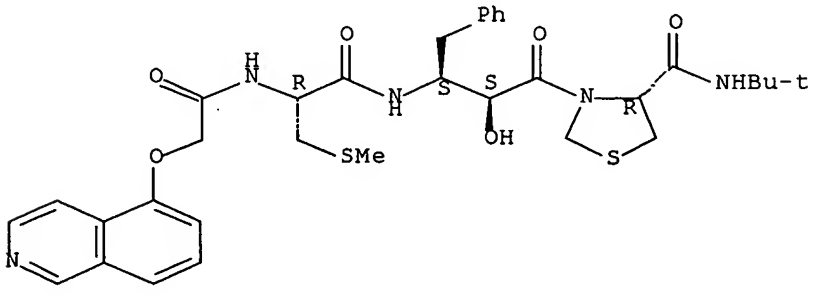
IT **147318-81-8P**

RL: PNU (Preparation, unclassified); PREP (Preparation)
(intermediates for HIV protease **inhibitor**; preparation of optically active allophenylnorstatin derivs. via asym. hydrogenation of phenylhalooxobutyric ester)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

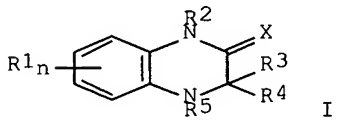
Absolute stereochemistry.



L31 ANSWER 37 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:601709 HCAPLUS Full-text
DOCUMENT NUMBER: 125:238651
TITLE: Use of quinoxalines and protease inhibitors in a composition for the treatment of AIDS and/or HIV infections
INVENTOR(S): Paessens, Arnold; Blunck, Martin; Riess, Guenther; Kleim, Joerg-Peter; Roesner, Manfred
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 728481	A2	19960828	EP 1996-102129	19960214 <--
EP 728481	A3	19980708		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 19506742	A1	19960829	DE 1995-19506742	19950227 <--
AU 9645615	A1	19960905	AU 1996-45615	19960220 <--
AU 710158	B2	19990916		
CA 2170222	AA	19960828	CA 1996-2170222	19960223 <--
FI 9600850	A	19960828	FI 1996-850	19960223 <--
JP 08245392	A2	19960924	JP 1996-60286	19960223 <--
IL 117247	A1	20001031	IL 1996-117247	19960223 <--
NO 9600775	A	19960828	NO 1996-775	19960226 <--
ZA 9601516	A	19960903	ZA 1996-1516	19960226 <--
BR 9600809	A	19971223	BR 1996-809	19960226 <--
CN 1141196	A	19970129	CN 1996-102709	19960227 <--

PRIORITY APPLN. INFO.: DE 1995-19506742 A 19950227
OTHER SOURCE(S): MARPAT 125:238651
GI



I

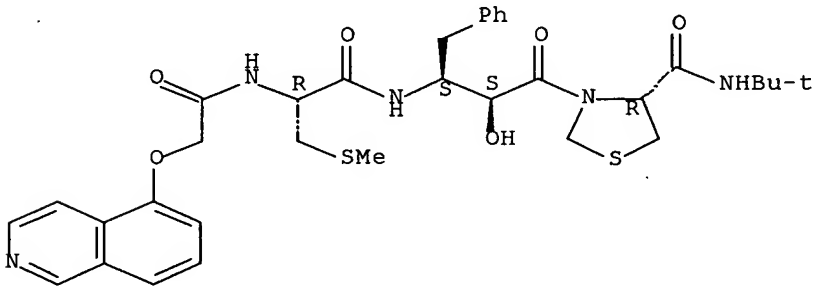
AB Combinations of a quinoxaline derivative [I; R1 = halo, OH, NO2, (substituted) amino, N3, CF3, CF3O, C1-8 alkyl, CN, (substituted) Ph, N-heterocyclyl, etc.; R2, R5 = H, OH, C1-6 alkoxy, aryloxy, C1-6 acyloxy, CN, (substituted) amino, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 alkynyl, (substituted) C3-8 cycloalk(en)yl, etc.; R3, R4 = H, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 cycloalk(en)yl, (substituted)aryl, etc.; or R3R4 or R3R5 complete a (substituted) ring; X = O, S, Se, NR2; n = 0-4] and a peptidomimetic protease inhibitor are useful for treatment of HIV infections and AIDS. Thus, I [R1 = 6-MeO, R2 = R3 = H, R4 = (S)-MeSCH2, R5 = i-PrO2C, X = S] (0.7-6 nM) and saquinavir (6-50 nM) synergistically inhibited syncytium formation in HIV-infected human lymphocytes in vitro.
IT **147318-81-8**, KNI 272

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of quinoxalines and protease **inhibitors** for treatment of AIDS and HIV infections)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

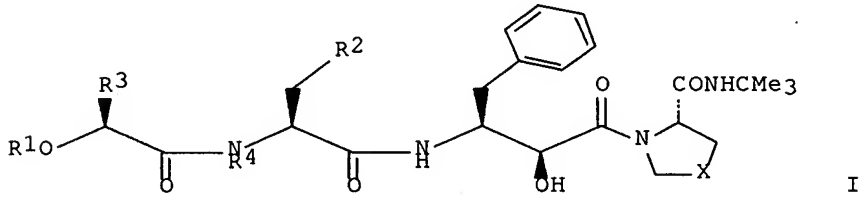
Absolute stereochemistry.



L31 ANSWER 38 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:567001 HCAPLUS Full-text
DOCUMENT NUMBER: 125:196384
TITLE: Synthesis of inhibitors of HIV proteinase
INVENTOR(S): Toyoda, Tatsuro; Fujioka, Norihiro; Fujiwara, Tamio; Hashimoto, Naofumi
PATENT ASSIGNEE(S): Shionogi Seiyaku KK, Japan; Shionogi and Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08165274	A2	19960625	JP 1994-306206	19941209 <--
JP 3605158	B2	20041222		

PRIORITY APPLN. INFO.: JP 1994-306206 19941209
OTHER SOURCE(S): MARPAT 125:196384
GI



I

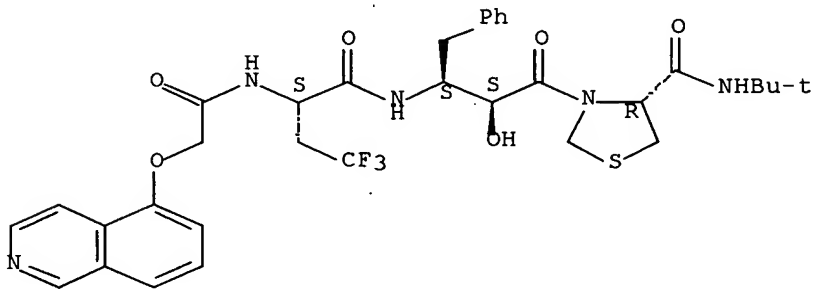
AB Compds. [I; R1 = (un)substituted aryl, (un)substituted hetero ring or (un)substituted heteroarylalkyl; R2 = F-substituted lower alkyl, F-substituted alkylthio; R3, R4= H, lower alkyl; X = S, SO, CH2] are effective in inhibiting proteinase of HIV and controlling AIDS.

IT **181128-28-9P 181128-30-3P 181128-32-5P 181128-34-7P 181128-40-5P 181128-44-9P 181128-46-1P 181128-47-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation as HIV proteinase **inhibitor**)

RN 181128-28-9 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[2-hydroxy-1-oxo-4-phenyl-3-[[4,4,4-trifluoro-2-[[(5-isoquinolinyloxy)acetyl]amino]-1-oxobutyl]amino]butyl]-, [4R-[3[2S*,3S*(S*)],4R*]]- (9CI) (CA INDEX NAME)

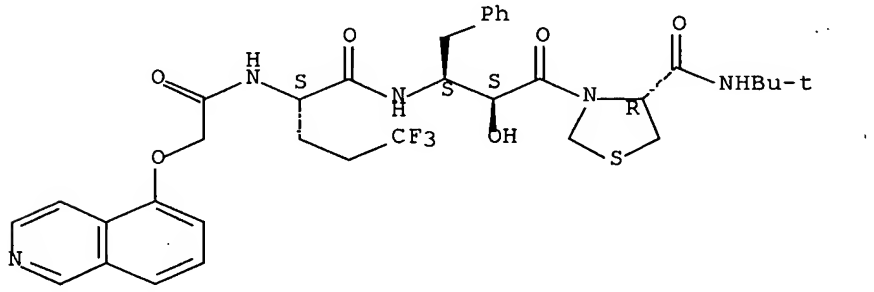
Absolute stereochemistry.



RN 181128-30-3 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[2-hydroxy-1-oxo-4-phenyl-3-[[5,5,5-trifluoro-2-[[(5-isoquinolinyloxy)acetyl]amino]-1-oxopentyl]amino]butyl]-, [4R-[3[2S*,3S*(S*)],4R*]]- (9CI) (CA INDEX NAME)

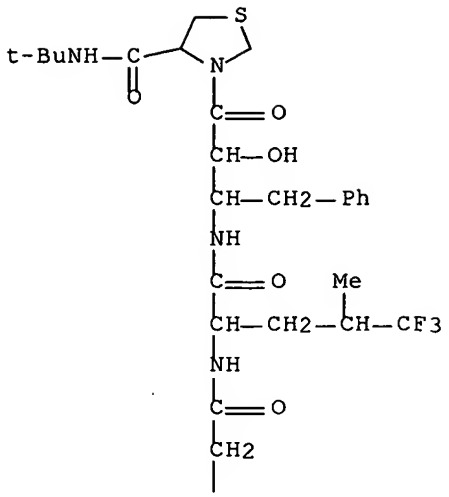
Absolute stereochemistry.



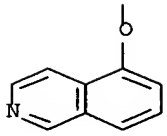
RN 181128-32-5 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[2-hydroxy-1-oxo-4-phenyl-3-[[5,5,5-trifluoro-2-[[(5-isoquinolinyloxy)acetyl]amino]-4-methyl-1-oxopentyl]amino]butyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

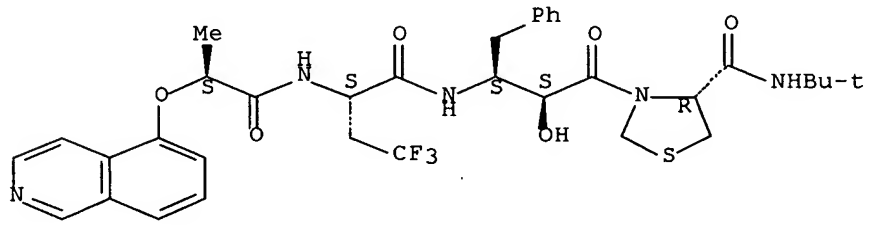


PAGE 2-A



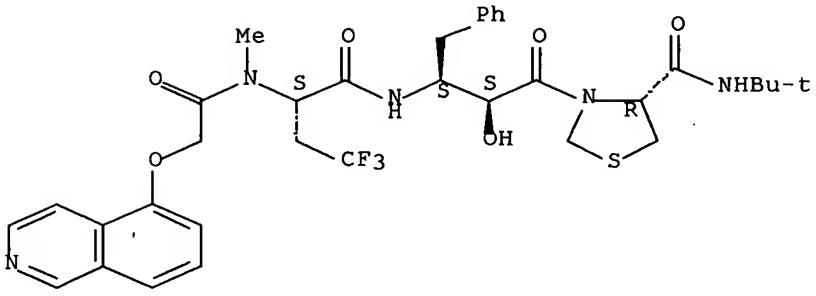
RN 181128-34-7 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[2-hydroxy-1-oxo-4-phenyl-3-[[4,4,4-trifluoro-2-[[2-(5-isoquinolinyloxy)-1-oxopropyl]amino]-1-oxobutyl]amino]butyl]-, [4R-[3[2S*,3S*[S*(S*)]],4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



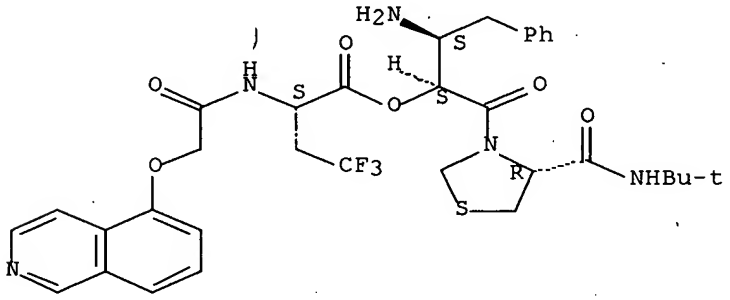
RN 181128-40-5 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[2-hydroxy-1-oxo-4-phenyl-3-[[4,4,4-trifluoro-2-[[(5-isoquinolinyloxy)acetyl]methylamino]-1-oxobutyl]amino]butyl]-, [4R-[3[2S*,3S*(S*)],4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



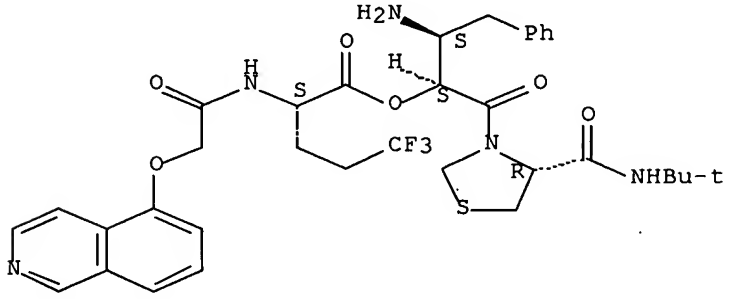
RN 181128-44-9 HCAPLUS
CN Butanoic acid, 4,4,4-trifluoro-2-[[(5-isoquinolinyloxy)acetyl]amino]-, 2-amino-1-[[4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenylpropyl ester, [4R-[3[1S*(S*),2S*],4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



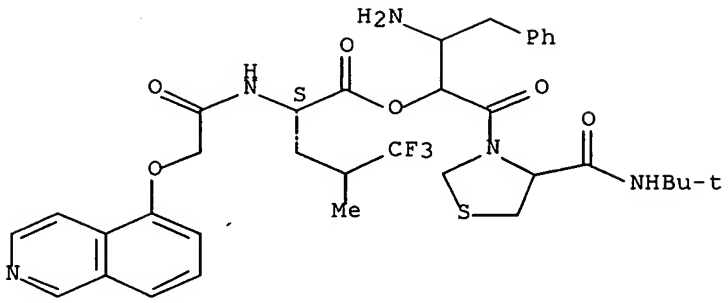
RN 181128-46-1 HCAPLUS
CN L-Norvaline, 5,5,5-trifluoro-N-[(5-isoquinolinyloxy)acetyl]-, 2-amino-1-[[4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenylpropyl ester, [4R-[3(1S*,2S*),4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 181128-47-2 HCAPLUS
CN L-Leucine, 5,5,5-trifluoro-N-[(5-isoquinolinyloxy)acetyl]-, 2-amino-1-[[4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 39 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:449440 HCAPLUS Full-text
DOCUMENT NUMBER: 125:115155
TITLE: Preparation of tripeptides with improved water solubility as prodrugs for HIV protease inhibitors
INVENTOR(S): Kimura, Tooru; Moriwaki, Hiroki; Kiso, Yoshiaki
PATENT ASSIGNEE(S): Hamari Yakuhin Kogyo Kk, Japan; Japan Enajii Kk
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08109180	A2	19960430	JP 1994-272953	19941011 <--
PRIORITY APPLN. INFO.:			JP 1994-272953	19941011

OTHER SOURCE(S): MARPAT 125:115155
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R = methylthiomethyl, methanesulfonylmethyl, carbamoylmethyl, optionally branched lower alkyl, (un)saturated 5- to 7-membered heterocyclyl; X = C, S; Y = 1-naphthyl, 5-isoquinolyl; n = 0,1] are prepared These peptide prodrugs show good water solubility, have themselves show no activity for inhibiting HIV protease, but undergo intramol. O→N acyl rearrangement at a physiol. pH and are converted into the corresponding active tripeptides (II) after oral administration, and thereby are expected for improving bioavailability through oral administration. Thus, (S)-tert-butoxycarbonyl-L-β-methylthioalanine (Boc-Mta-OH) was condensed with Z-(2S,3S)-AHPBA-Thz-NHCMe3 [Z = PhCH2, AHPBA = 3-amino-2-hydroxy-4-phenylbutyric acid, Thz = (S)-1,3-thiazolidine- 4-carboxylic acid] using DCC and 4-dimethylaminopyridine in CH2Cl2 to give an intermediate (III; R1 = Z, R2 = Boc), which was deprotected with HCl in dioxane and condensed with 5-isoquinolyloxyacetic acid using DCC and Et3N in CH2Cl2 to give a precursor III (R1 = Z, R2 = Q). The latter compound was dissolved in di-Me sulfide and anisole, cooled to -5°, treated with CF3CO2H at ≤10°, stirred at ≤10° for 1 h

and at room temperature for 20 h, distilled in vacuo by coevaporation with Et2O, redissolved in toluene and EtOAc, and treated dropwise with 4 N HCl in dioxane at 0° to give 70.4% III. HCl (R1 = H, R2 = Q) (IV). A solution (50 μL) of this tripeptide IV (1 mg) in a physiol. saline was added to a phosphate buffer physiol. saline (pH 7.4, 300 μL) and incubated at 37°. IV underwent O→N acyl rearrangement to form the corresponding active peptide II (Y = 5-isoquinolyl, R = MeSCH2) in 43.5, 68.0, 85.2, 93.6, and 99.5% yield after 1, 2, 5, 15, and 60 min, resp. The half life of IV in a phosphate buffer was 3 h, 12 min, and 25 s at pH 4.9, 5.5, and 8.0, resp., and the solubility of IV in H2O was >500 mg/mL vs. 0.084 mg/mL for the active peptide. IV showed IC50 of 6.5 nM against HIV protease.

IT **147318-81-8P 156880-90-9P 169752-83-4P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

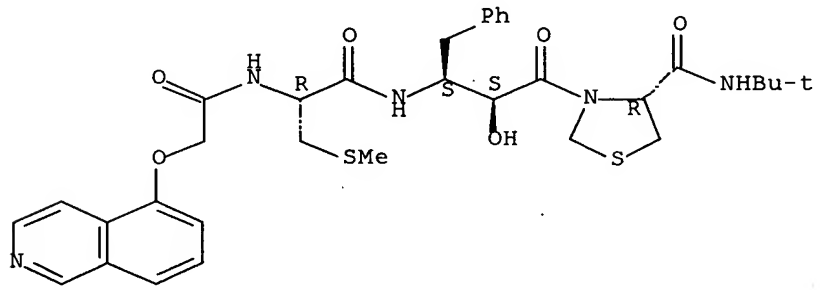
(preparation of tripeptides and their prodrugs with improved water solubility as

HIV protease **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

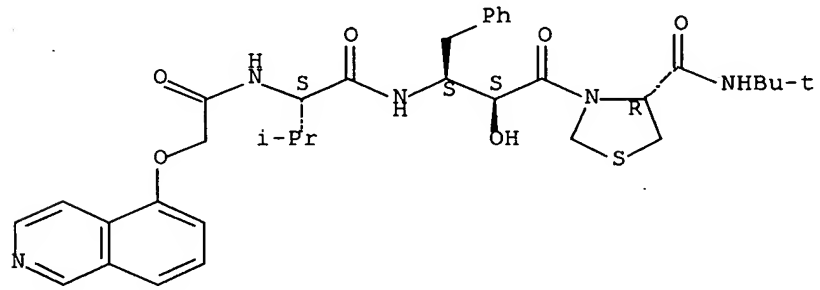
Absolute stereochemistry.



RN 156880-90-9 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-1-oxobutyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

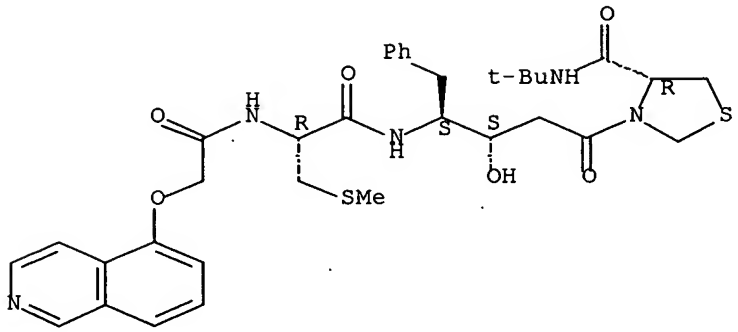


RN 169752-83-4 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[3-hydroxy-4-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-5-

phenylpentyl]-, [4R-[3[3S*,4S*(R*)],4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

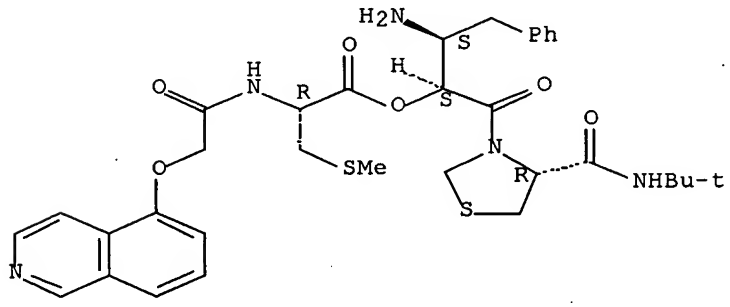


IT **169752-81-2P 178986-84-0P 179093-80-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tripeptides with improved water solubility as prodrugs for HIV
protease **inhibitors**)

RN 169752-81-2 HCAPLUS

CN L-Cysteine, N-[(5-isoquinolinyloxy)acetyl]-S-methyl-, (1S,2S)-2-amino-1-[[(4R)-4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenylpropyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

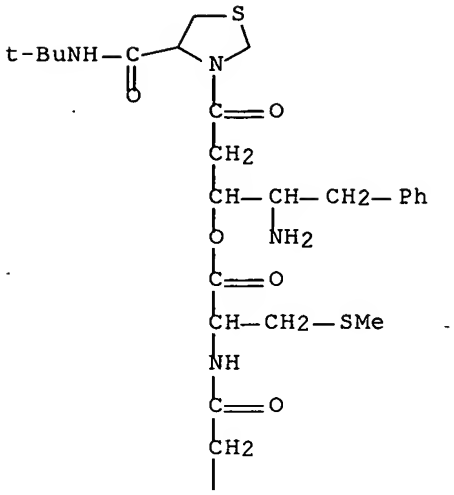
RN 178986-84-0 HCAPLUS

CN L-Cysteine, N-[(5-isoquinolinyloxy)acetyl]-S-methyl-, 2-amino-1-[2-[4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]-2-oxoethyl]-3-phenylpropyl ester, [4R-[3(1S*,2S*),4R*]]-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

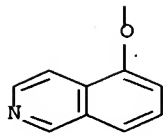
CM 1

CRN 178986-83-9
CMF C34 H43 N5 O6 S2

PAGE 1-A

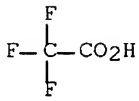


PAGE 2-A



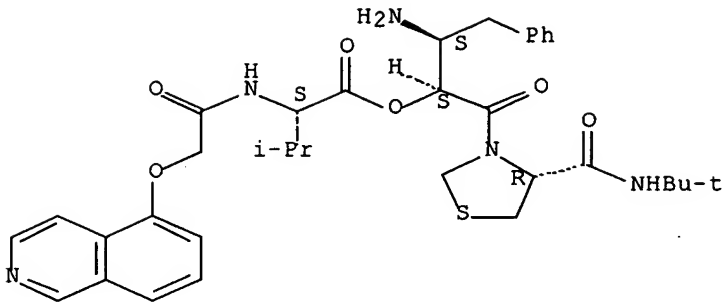
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 179093-80-2 HCAPLUS
CN L-Valine, N-[(5-isoquinolinyloxy)acetyl]-, (1S,2S)-2-amino-1-[[(4R)-4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenylpropyl ester, dihydrochloride (9CI) (CA INDEX NAME)

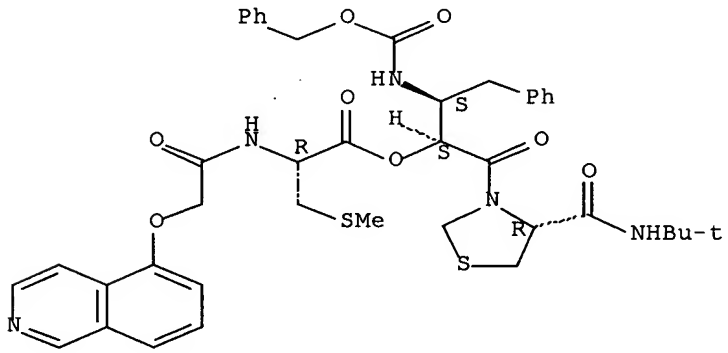
Absolute stereochemistry. Rotation (-).



●2 HCl

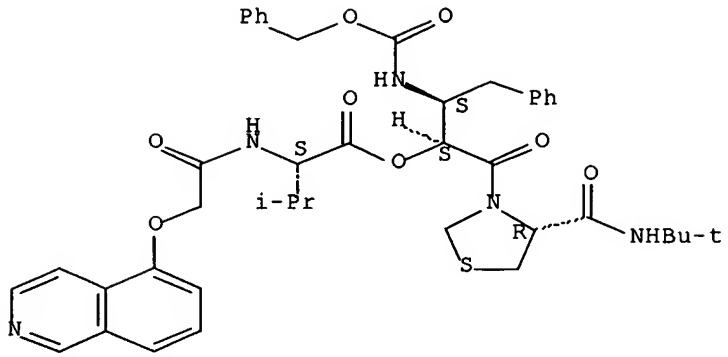
IT **169752-80-1P 178986-90-8P 178986-92-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tripeptides with improved water solubility as prodrugs for HIV
protease **inhibitors**)
RN 169752-80-1 HCAPLUS
CN L-Cysteine, N-[(5-isoquinolinyloxy)acetyl]-S-methyl-, (1S,2S)-1-[[(4R)-4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenyl-2-[[(phenylmethoxy)carbonyl]amino]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



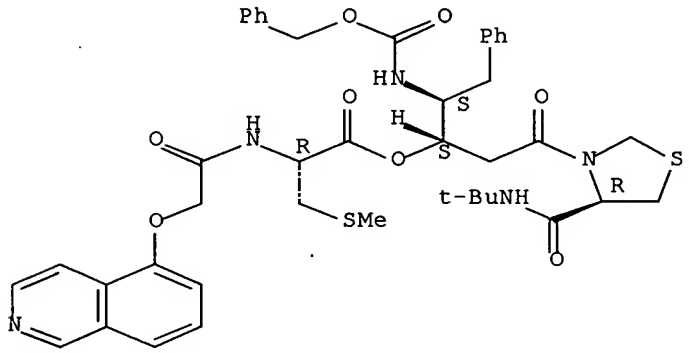
RN 178986-90-8 HCAPLUS
CN L-Valine, N-[(5-isoquinolinyloxy)acetyl]-, (1S,2S)-1-[[(4R)-4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]carbonyl]-3-phenyl-2-[[(phenylmethoxy)carbonyl]amino]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 178986-92-0 HCAPLUS
CN L-Cysteine, N-[(5-isoquinolinyloxy)acetyl]-S-methyl-, 1-[2-[4-[[(1,1-dimethylethyl)amino]carbonyl]-3-thiazolidinyl]-2-oxoethyl]-3-phenyl-2-[[(phenylmethoxy)carbonyl]amino]propyl ester, [4R-[3(1S*,2S*),4R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



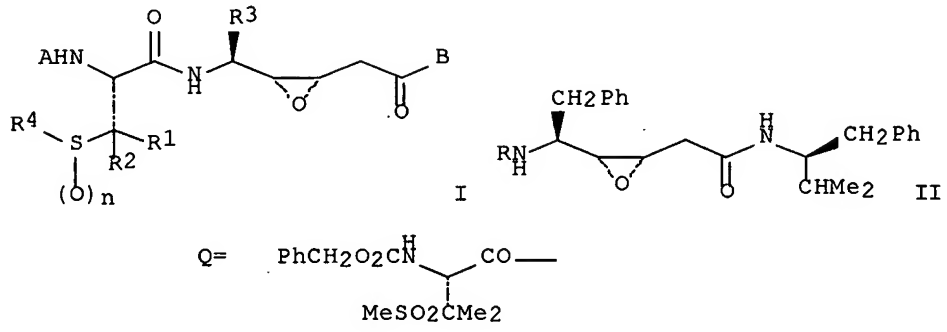
L31 ANSWER 40 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:171803 HCAPLUS Full-text
DOCUMENT NUMBER: 124:233139
TITLE: Preparation of sulfonylamino acid amides containing cis-epoxide as irreversible HIV protease inhibitors
INVENTOR(S): Yoon, Heungsik; Choy, Nakyen; Kim, Sung Chun; Choi, Ho II; Son, Young Chan; Park, Chi Hyo; Moon, Kwang-Yul; Jung, Wonhee; Kim, Chung Ryeol; et al.
PATENT ASSIGNEE(S): IG Chemical Ltd., S. Korea
SOURCE: Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 687675	A2	19951220	EP 1995-108908	19950609 <--
EP 687675	A3	19960306		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

KR 125117	B1	19971205	KR 1994-13423		19940615 <--
JP 08193077	A2	19960730	JP 1995-172733		19950615 <--
JP 2987313	B2	19991206			
PRIORITY APPLN. INFO.:			KR 1994-13423	A	19940615
OTHER SOURCE(S):	MARPAT 124:233139				

GI

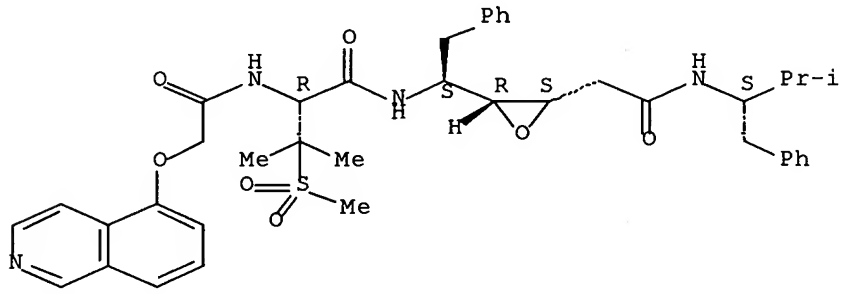


AB Novel cis-epoxide compds. [I; R1, R2 = H, alkyl; R3 = (un)substituted aryl or alkyl; R4 = H, C1-4 alkyl; n = 0,1,2; A = (X)(Y)mR5, NR6R7, ZCHR8R9; wherein X = CO, COCO, CO, SO2, CS; Y = O, CH2, NH, NMe; m = 0,1; R5 = heterocyclyl, straight or branched or cyclic C1-8 alkyl or alkoxy, heterocyclylalkyl, cycloalkylalkyl, arylalkoxy; R6 = straight or branched C1-8 alkyl, cycloalkyl, cycloalkylalkyl; R7 = H, alkyl; Z = O, NH, NMe; R8, R9 = alkyl optionally substituted by aromatic hydrocarbyl or cycloalkyl, C3-8 cycloalkyl, aryl], useful for treating or preventing diseases caused by HIV infection, are prepared The novel HIV protease inhibitor I has a specific structure to form a stable bonding with the enzyme active site, which entails a highly enhanced irreversible inhibition against HIV protease. An anti-AIDS or immunomodulator contains a therapeutically effective amount of said cis-epoxide I. Thus, (S)-5-[(N- benzyloxycarbonyl)amino]-6-phenyl-(cis)-3-hexene-1-carboxylic acid was condensed with (S)-2-amino-3-methyl-1-phenylbutane using N-ethyl-N'-(3-(dimethylamino)propyl)carbodiimide hydrochloride (EDC) and HOBT in DMF followed by epoxidn. with m-chloroperbenzoic acid in CH2Cl2 to give the cis-epoxide (II; R = PhCH2O2C), which was hydrogenolyzed in the presence of 10% Pd-C in MeOH under an atmospheric of H, coupled with N-benzyloxycarbonyl-β-(S-methyl)-L-valine using EDC and HOBT in DMF , and oxidized with m-chloroperbenzoic acid in CH2Cl2 to give the title compound II (R = Q). The latter compound in vitro inhibited HIV protease with the inhibition constant Kina/Ki min-1M-1 109-1010 (Kina = a rate constant indicating rate of chemical reaction forming covalent bond between an enzyme and an inhibitor in Michaelis-Menten complex; Ki = an inhibition constant indicating the dissociation rate of Michaelis-Menten complex into an enzyme and an inhibitor) and in vitro showed IC50 of 1 nM for inhibiting the HIV-1 infection of H9 or Sup T1 cell lines.

IT **174562-56-2P 174562-57-3P 174562-58-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylamino acid amides containing cis-epoxide as irreversible
HIV protease **inhibitors** for treating AIDS)

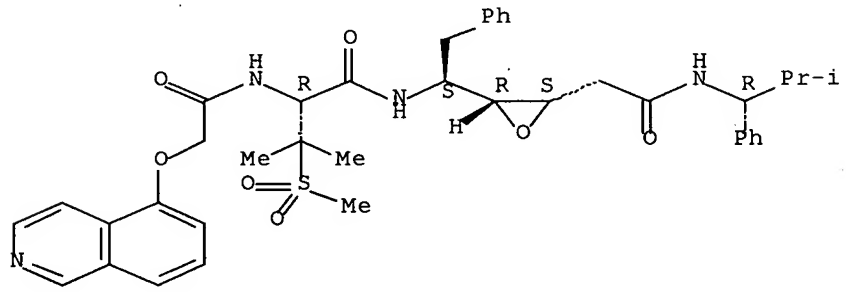
RN 174562-56-2 HCAPLUS
CN Oxiraneacetamide, 3-[1-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-2-phenylethyl]-N-[2-methyl-1-(phenylmethyl)propyl]-, [2S-[2α(R*),3α[R*(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



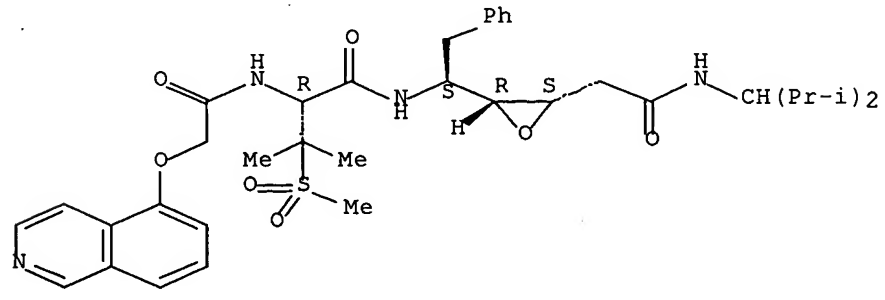
RN 174562-57-3 HCAPLUS
CN Oxiraneacetamide, 3-[1-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-2-phenylethyl]-N-(2-methyl-1-phenylpropyl)-, [2S-[2α(S*),3α[R*(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174562-58-4 HCAPLUS
CN Oxiraneacetamide, 3-[1-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-3-(methylsulfonyl)-1-oxobutyl]amino]-2-phenylethyl]-N-[2-methyl-1-(1-methylethyl)propyl]-, [2S-[2α,3α[R*(S*)]]]- (9CI) (CA INDEX NAME)

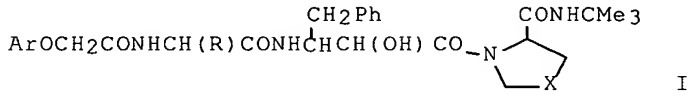
Absolute stereochemistry.



L31 ANSWER 41 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:128450 HCAPLUS Full-text
DOCUMENT NUMBER: 124:242317
TITLE: Preparation of anti-AIDS agents containing 3-amino-2-hydroxy-4-butanoic acid derivatives and the oral preparations
INVENTOR(S): Takeuchi, Shohachi; Hiratsuka, Sashichi; Fujisawa, Naoki
PATENT ASSIGNEE(S): Japan Enajii Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07324032	A2	19951212	JP 1994-139429	19940530 <--

PRIORITY APPLN. INFO.: JP 1994-139429 19940530
OTHER SOURCE(S): MARPAT 124:242317
GI



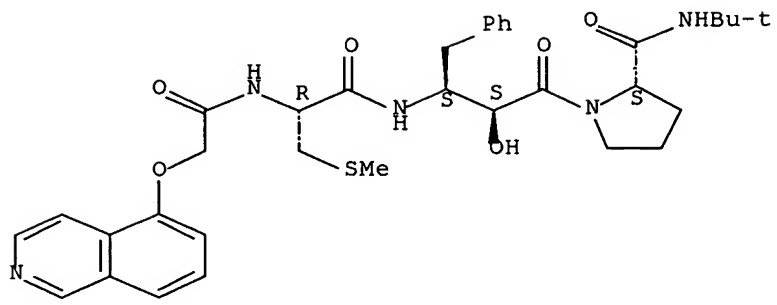
I

AB The anti-AIDS agents are prepared by coating of solid acidic substances with fine powders of the title derivs. I (Ar = 5-isoquinolinyl, 3-pyridyl; R = CH2SMe, CHMe2; X = S, CH2). Anti-AIDS prepns. containing the above composite powders are also claimed. The prepns. for oral administration show improved bioavailability. Citric acid powder (average particle size 7 μm) (200 parts) was mixed with 100 parts powder of (R)-N-tert-butyl-3-[(2S,3S)- 2-hydroxy-3-N-[(R)-2-N-(5-isoquinolyloxyacetyl)amino-3- methlthiopropanoyl]amino-4-phenylbutanoyl]1,3-thiazolidine-4-carboxamide (II; average particle size 2 μm) using a hybridizer to give composite powder. A mixture of 450 parts composite powder and 2.5 parts light SiO2 was made into granules, which was mixed with excipients and the mixture was made into enteric-coated tablets containing 150 mg II/per tablet. The enteric-coated tablet was p.o. administered to beagles to show bioavailability 20.42%, vs. 12.43% for a control tablet prepared from granules obtained by direct mixing of II 150, citric acid 300, and SiO2 2.5 parts.

IT **174730-46-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(oral AIDS **inhibitors** prepared by coating of acidic substance powders with aminohydroxybutanoic acid derivs. for improved bioavailability)

RN 174730-46-2 HCAPLUS
CN L-Prolinamide, N-[(5-isoquinolinyloxy)acetyl]-S-methyl-L-cysteinyl-(2S,3S)-2-hydroxy-4-phenyl-3-aminobutanoyl-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 42 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:967537 HCAPLUS Full-text
DOCUMENT NUMBER: 124:15515
TITLE: Oral preparations of slightly soluble drugs containing propylene glycol and absorbefacients
INVENTOR(S): Takada, Kanji
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07242535	A2	19950919	JP 1994-33851	19940303 <--

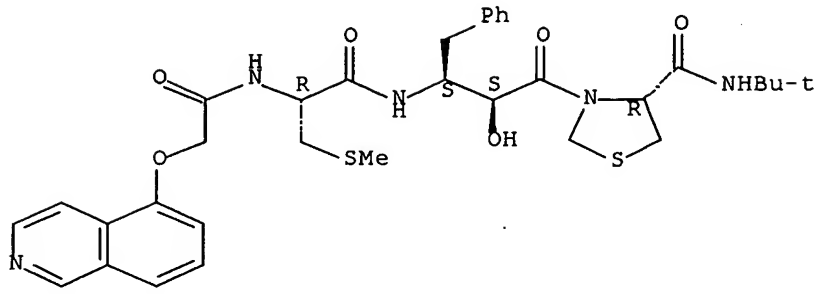
PRIORITY APPLN. INFO.: JP 1994-33851 19940303

AB Oral prepns. for highly lipophilic and slightly water-soluble drugs contain propylene glycol (I) and ≥1 the other absorbefacients. Capsules coated inside with a substance, which is insol. in I, containing the above oral prepns. are also claimed. Enteric-coated capsules containing the above oral prepns. are also claimed. Cyclosporin A (50 mg) was dissolved in a mixture of 0.8 mL I and 5- mg HCO 60 and the mixture was encapsulated with a gelatin capsule, which was previously coated inside with an Et cellulose solution, and the air in the cavity was replaced with I containing CHO 60 to give a capsule. The capsule was administered to a beagle dog to show higher AUC than a control capsule containing powder of cyclosporin A.

IT **147318-81-8**, KNI 272 **147384-69-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(AIDS **inhibitor**; oral prepns. of lipophilic and slightly water-soluble drugs containing propylene glycol and absorbefacients)

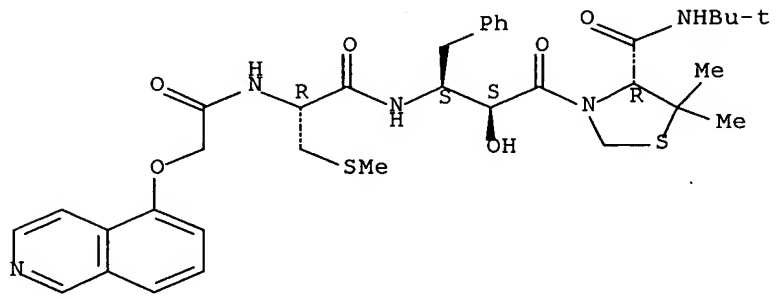
RN 147318-81-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 147384-69-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

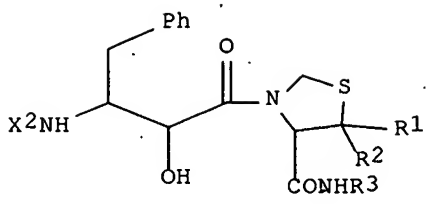
Absolute stereochemistry.



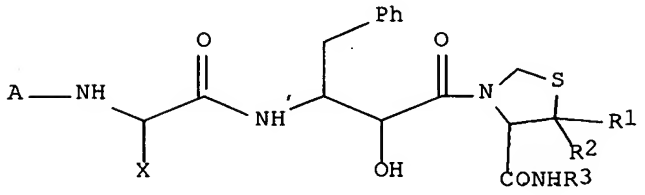
L31 ANSWER 43 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:339426 HCAPLUS Full-text
DOCUMENT NUMBER: 122:133859
TITLE: preparation of peptides derivatives as intermediates for HIV protease inhibitors
INVENTOR(S): Maeda, Sadayuki; Moriwaki, Hiroki; Mitsumoto, Tsutomu; Kisanuki, Junji; Kato, Ryohei; Maeda, Hiroshi; Takahashi, Osamu; Kiso, Yoshiaki
PATENT ASSIGNEE(S): Japan Enajii Kk, Japan; Hamari Yakuhin Kogyo Kk
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06220031	A2	19940809	JP 1993-28546	19930125 <--
PRIORITY APPLN. INFO.:			JP 1993-28546	19930125

OTHER SOURCE(S): CASREACT 122:133859; MARPAT 122:133859
GI



I



II

AB 1,3-Thiazolidine-4-carboxamides [I; R1, R2 = alkyl, H; R3 = alkyl; X2 = H2N-CHX-CO-] are reacted with A-NH-CHX-CO2H [A = amino protecting group] and (PhO)2P(O)B [B = azido, (un)substituted] to give the peptide derivs. II, useful as intermediates for HIV protease inhibitors. Thus, H-AHPBA-Thz-NH-tBu [AHPBA = 3-amino-2-hydroxy-4-phenylbutanoic acid residue; Thz = thiazolidine-4-carboxylic acid residue] (preparation given) was treated with BOC-Mta-OH [Mta = methylthioalanine residue] in DMF containing diphenylphosphoryl azide (DPPA) and Et3N at ≤8° overnight to give, after deprotection, H-Mta-AHPBA-Thz-tBu, which was reacted with Qoa-OH [Qoa = 5-isoquinolinyloxyacetic acid residue] in DMF containing DPPA and Et3N at 0° for 1 h to give Qoa-Mta-AHPBA-Thz-tBu.

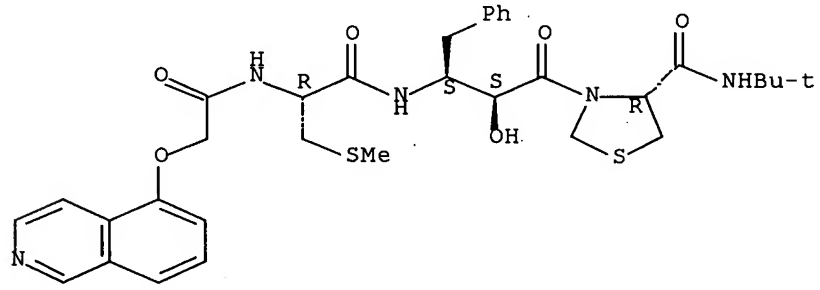
IT **147318-81-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides derivs. as intermediates for HIV protease **inhibitors**)

RN 147318-81-8 HCAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 44 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:701322 HCAPLUS Full-text
DOCUMENT NUMBER: 121:301322

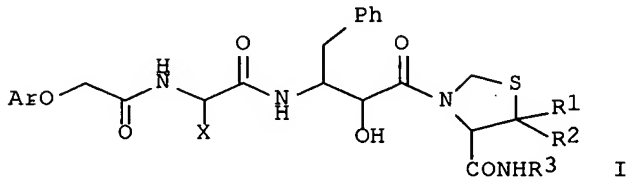
TITLE: Processes for producing peptide derivative HIV protease inhibitors.
INVENTOR(S): Mimoto, Tsutomu; Kisanuki, Sumitsugu; Takahasihi, Osamu; Kiso, Yoshiaki
PATENT ASSIGNEE(S): Nikko Kyodo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 574135	A1	19931215	EP 1993-303644	19930511 <--
EP 574135	B1	19981118		
R: DE, FR, GB				
JP 05310687	A2	19931122	JP 1992-192653	19920513 <--
JP 06247948	A2	19940906	JP 1992-192654	19920513 <--
JP 06192246	A2	19940712	JP 1992-323599	19921109 <--

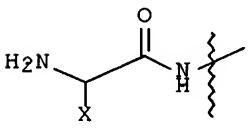
PRIORITY APPLN. INFO.:

JP 1992-192653	A	19920513
JP 1992-192654	A	19920513
JP 1992-157459	A	19920525
JP 1992-315640	A	19921030
JP 1992-323599	A	19921109

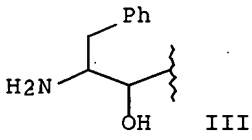
OTHER SOURCE(S): MARPAT 121:301322
GI



I



II



III

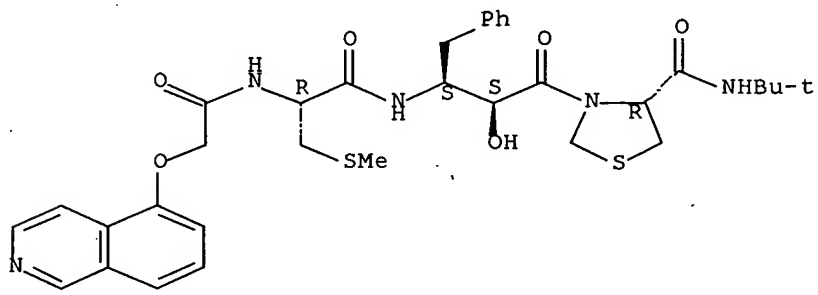
AB Peptide derivs. [I; R1, R2 alkyl, H; R3 = alkyl; X = methylthiomethyl, methanesulfonylmethyl, carbamoylmethyl, alkyl; Ar = aryl, heteroaryl], were prepared by (1) condensation of peptide derivative II with ArOCH2CO2H, or (2) coupling of peptide derivative III with A4NHCHXCO2H (A4 = ArOCH2CO). I are useful as HIV protease inhibitors (no data). Thus, BOC-Mta-AHPBA-Thz-NHBu-t [Mta = (R)-2-amino-3-methylthiopropionate, AHPBA = (2S,3S)-3-amino-2-hydroxy-4-phenylbutanoate, Thz = (R)-1,3-thiazolidine- 4-carboxylate] (preparation given) was stirred with 4 M HCl in dioxane; the reaction residue was treated with 5-isoquinolinyloxyacetic acid (Qoa-OH), Et3N, DCC, and hydroxybenzotriazole in DMF to give 95% Qoa-Mta-AHPBA-Thz-NHBu-t.

IT **147318-81-8P 147384-69-8P 156880-90-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)
(preparation of, as HIV protease **inhibitor**)

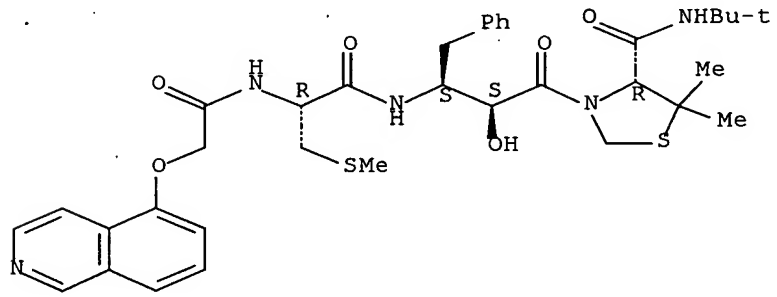
RN 147318-81-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



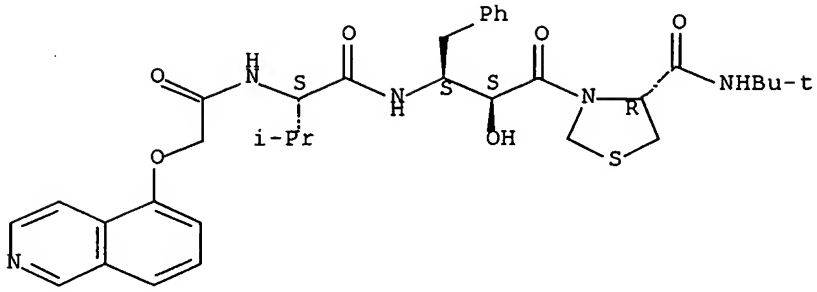
RN 147384-69-8 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



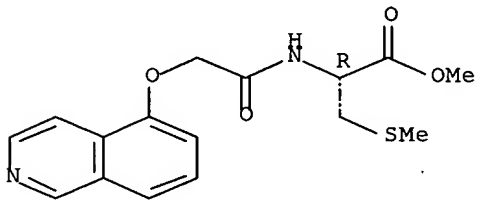
RN 156880-90-9 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2S)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-methyl-1-oxobutyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



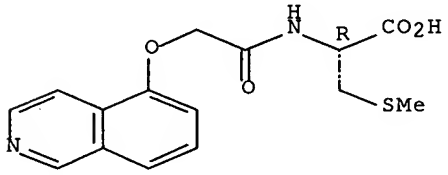
IT **158941-61-8P 158941-62-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for peptide derivative HIV protease **inhibitor**)
RN 158941-61-8 HCAPLUS
CN L-Cysteine, N-[(5-isoquinolinyloxy)acetyl]-S-methyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 158941-62-9 HCAPLUS
CN L-Cysteine, N-[(5-isoquinolinyloxy)acetyl]-S-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 45 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:290088 HCAPLUS Full-text
DOCUMENT NUMBER: 120:290088
TITLE: Inhibitors of metazoan parasite proteases
INVENTOR(S): Cohen, Fred Ehrenkranz; McKerrow, James Hobson; Ring, Christine Sun Young; Rosenthal, Philip Jon; Kenyon, George Lommel; Li, Zhe
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9406280	A1	19940331	WO 1993-US8708	19930913 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9349230	A1	19940412	AU 1993-49230	19930913 <--
JP 08502048	T2	19960305	JP 1994-508279	19930913 <--
EP 752813	A1	19970115	EP 1993-921592	19930913 <--
EP 752813	B1	20021211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 229331	E	20021215	AT 1993-921592	19930913
ES 2183817	T3	20030401	ES 1993-921592	19930913
PT 752813	T	20030430	PT 1993-921592	19930913
US 5610192	A	19970311	US 1995-387760	19950328 <--
US 5739170	A	19980414	US 1995-413337	19950330 <--
US 6548521	B1	20030415	US 2000-628080	20000728

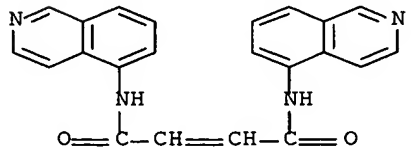
PRIORITY APPLN. INFO.:	US 1992-943925	A2 19920911
	WO 1993-US8708	W 19930913
	US 1995-387760	A2 19950328
	US 1995-413337	A1 19950330
	US 1997-801	A1 19971230

OTHER SOURCE(S): MARPAT 120:290088

AB Compns. and methods for treating a patient infected with a metazoan parasite by inhibiting the enzymic action of the metazoan parasite protease are claimed. These compns. and methods have particular utility in the treatment of schistosomiasis, malaria, and other infectious diseases. The compns. contain at least one metazoan protease inhibitor compound containing specific structural elements which bind to the S2 subsite and at least one of the S1 and S1' subsites of the metazoan parasite protease. The protease inhibitors generally include at least two homoarom. or heteroarom. ring systems, each comprising 1-3 rings, joined together by suitable linkers. For example, oxalic bis(2-hydroxy-1- phenylmethylene)hydrazide was prepared and its inhibitory action against trophozoite cysteine protease was demonstrated.

IT **155062-60-5**
RL: BIOL (Biological study)
(metazoan protease **inhibitor**, malaria and schistosomiasis treatment with)

RN 155062-60-5 HCAPLUS
CN 2-Butenediamide, N,N'-di-5-isoquinolinyl- (9CI) (CA INDEX NAME)



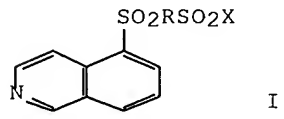
L31 ANSWER 46 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:134303 HCAPLUS Full-text
DOCUMENT NUMBER: 120:134303

TITLE: Preparation of 5-isoquinolinesulfonamides as protein kinase inhibitors
INVENTOR(S): Levi, Silvio; Gromo, Gianni; Maoret, Tiziana; Sala, Alberto
PATENT ASSIGNEE(S): Italfarmaco S.p.A., Italy
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9313072	A1	19930708	WO 1992-EP2869	19921211 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9332561	A1	19930728	AU 1993-32561	19921211 <--
ZA 9209768	A	19930614	ZA 1992-9768	19921217 <--

PRIORITY APPLN. INFO.: IT 1991-MI3431 A 19911220
WO 1992-EP2869 A 19921211

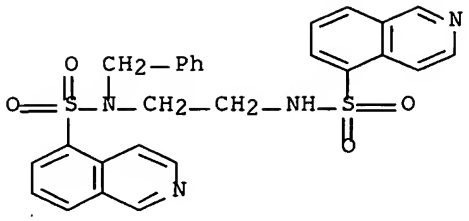
OTHER SOURCE(S): MARPAT 120:134303
GI



I

AB Title compds. I [R = R1NR3NR2, bivalent residue of a 4- to 8-membered heterocyclic group; R1, R2 = H, Me, Et, (un)branched C3-6 alkyl, (un)substituted PhCH2; R3 = (un)branched (un)substituted C2-6 alkylene; X = (un)substituted isoquinoline group, (un)substituted naphthyl], useful for the treatment of cardiovascular diseases (no data), inflammatory and immune diseases (no data), in oncol. (no data), and in organ transplants (no data), were prepared Thus, 5-isoquinolinesulfonyl chloride hydrochloride was condensed with N-methylethylenediamine, producing N-methyl-N,N'-bis(5-isoquinolinesulfonyl)ethylenediamine hydrochloride (II). II at 100 μM demonstrated 100% protein kinase A inhibitory activity and 80% protein kinase C inhibitory activity.

IT **152877-15-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and protein kinase-**inhibiting** activity of)
RN 152877-15-1 HCAPLUS
CN 5-Isoquinolinesulfonamide, N-[2-[(5-isoquinolinylsulfonyl)amino]ethyl]-N-(phenylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

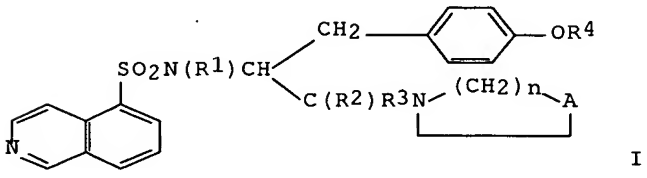


●2 HCl

L31 ANSWER 47 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:641393 HCAPLUS Full-text
DOCUMENT NUMBER: 119:241393
TITLE: Isoquinoline sulfonamide derivatives for anti-ulcer agents
INVENTOR(S): Hidaka, Hiroyoshi; Ishikawa, Tomohiko
PATENT ASSIGNEE(S): Japan
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5244895	A	19930914	US 1992-883344	19920515 <--
PRIORITY APPLN. INFO.:			JP 1991-8580 A	19910515
OTHER SOURCE(S):	MARPAT 119:241393			

GI

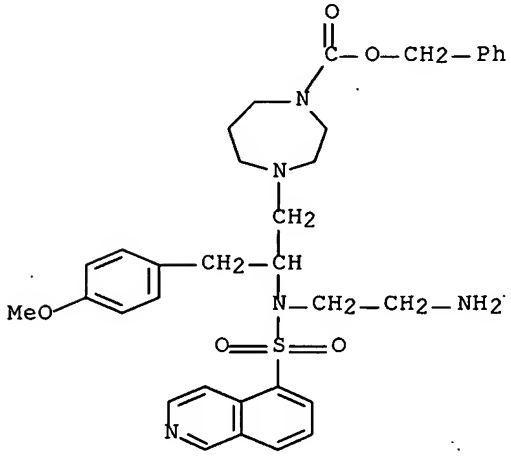


I

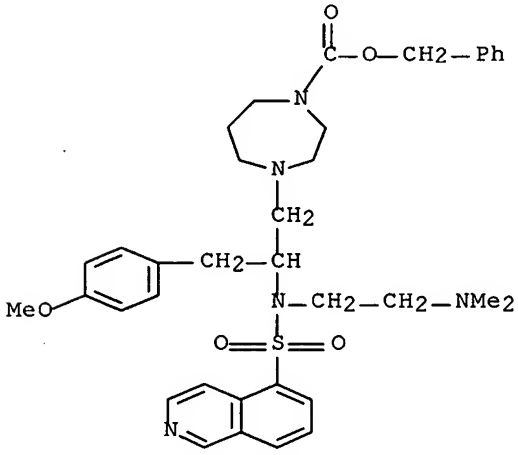
AB The anti-ulcer agents of the invention are I [R1 = H, (substituted) C1-2 alkyl; R2, R3 = H or together form oxo; R4 = H, Me, isoquinoline sulfonyl; n = 2, 3; A = NR5 CHR5 (R5 = (substituted) Ph, (substituted) benzyloxycarbonyl] or a physiol. allowable acid addition salt thereof. Twelve specific I are claimed; and preparation of 3 I is described. Thus, N-[N,O-bis(5-isoquinoline sulfonyl)-N-methyl-tyrosyl]-4-phenylpiperazine (II) (preparation given) and 15 other I were tested in an anti-gastric juice secretion test and an anti-aspirin ulcer test. Tablet and injection formulations of II phosphate are included.

IT **146135-09-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for ulcer **inhibitor**)
RN 146135-09-3 HCAPLUS

CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[2-[(2-aminoethyl)(5-isoquinolinylsulfonyl)amino]-3-(4-methoxyphenyl)propyl]hexahydro-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT **146345-11-1**
RL: BIOL (Biological study)
(ulcer **inhibitor**)
RN 146345-11-1 HCAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[2-[[2-(dimethylamino)ethyl](5-isoquinolinylsulfonyl)amino]-3-(4-methoxyphenyl)propyl]hexahydro-, phenylmethyl ester (9CI) (CA INDEX NAME)



L31 ANSWER 48 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:409161 HCAPLUS Full-text
DOCUMENT NUMBER: 119:9161
TITLE: HIV protease inhibitors
INVENTOR(S): Mimoto, Tsutomu; Hattori, Naoko; Nagano, Yuuichi; Shintani, Makoto; Kiso, Yoshiaki
PATENT ASSIGNEE(S): Nippon Mining Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 86 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 490667	A2	19920617	EP 1991-311549	19911211 <--
EP 490667	A3	19930505		
EP 490667	B1	19990609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2056911	AA	19920612	CA 1991-2056911	19911204 <--
CA 2056911	C	19980922		
JP 05170722	A2	19930709	JP 1991-348705	19911205 <--
JP 2700511	B2	19980121		
AU 9188900	A1	19920618	AU 1991-88900	19911206 <--
AU 653972	B2	19941020		
ZA 9109721	A	19921230	ZA 1991-9721	19911210 <--
FI 9105819	A	19920612	FI 1991-5819	19911211 <--
FI 108113	B1	20011130		
AT 181080	E	19990615	AT 1991-311549	19911211 <--
ES 2134764	T3	19991016	ES 1991-311549	19911211 <--
NO 9200023	A	19920727	NO 1992-23	19920102 <--
NO 305085	B1	19990329		
US 6313094	B1	20011106	US 1994-246843	19940520 <--
US 6329502	B1	20011211	US 1995-378057	19950125 <--

PRIORITY APPLN. INFO.:

JP 1990-409673	A	19901211
JP 1991-25755	A	19910125
JP 1991-89976	A	19910328
JP 1991-169174	A	19910614
JP 1991-304043	A	19911023
US 1991-804590	B2	19911210
US 1993-44043	B1	19930408

OTHER SOURCE(S): MARPAT 119:9161

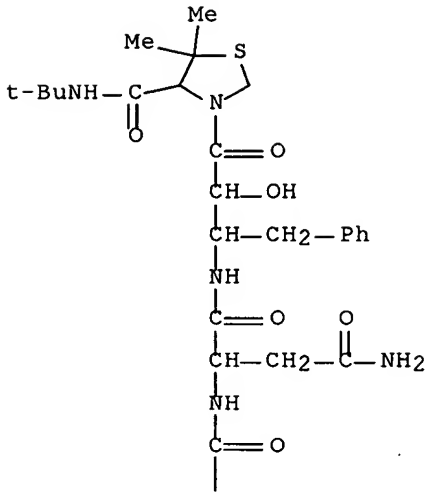
AB A-B1-B2-B3-NHCHR1CH(OH)CO-B4-B5-B6-XR2R3 [A = H, N-protecting group; B1-B6 = (un)substituted amino acid residue, bond; R1 = (un)substituted alkyl, cycloalkyl, aryl, heterocyclic; R2, R3 = H (un)substituted hydrocarbon; X = N, O; R3 absent if X = O] (188 compds.) were prepared Thus, PhCH2CH2CO-Asn-X1-Pro-Ile-Val-NH2 [X1 = (2R,3S)-NHCH(CH2Ph)CH(OH)CO, I] was prepared by solid-phase synthesis. HIV protease treated with 1mM I showed 1.5% residual activity.

IT **143934-61-6P 143934-80-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and HIV protease-**inhibiting** activity of)

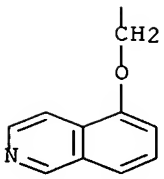
RN 143934-61-6 HCAPLUS

CN Butanediamide, N1-[3-[4-[[(1,1-dimethylethyl)amino]carbonyl]-5,5-dimethyl-3-thiazolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-[[(5-isoquinolinyloxy)acetyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

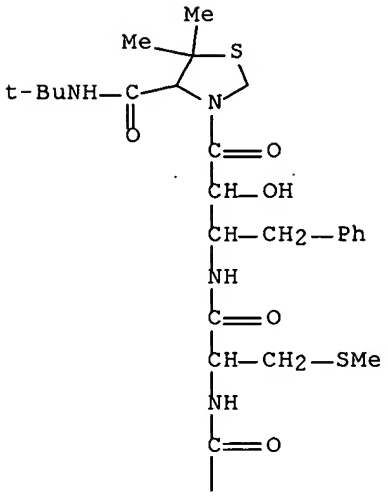


RN 143934-80-9 HCAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[2-hydroxy-3-[[2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-5,5-dimethyl-, monoacetate (salt) (9CI) (CA INDEX NAME)

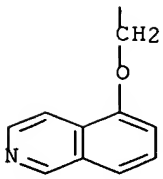
CM 1

CRN 143934-79-6
CMF C35 H45 N5 O6 S2

PAGE 1-A



PAGE 2-A



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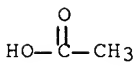
CRN 64-19-7
CMF C2 H4 O2



L31 ANSWER 49 OF 49 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:19985 HCAPLUS Full-text
DOCUMENT NUMBER: 96:19985
TITLE: Isoquinoline derivatives
INVENTOR(S): Barnish, Ian Thompson; Cross, Peter Edward; Dickinson, Roger Peter
PATENT ASSIGNEE(S): Pfizer Ltd., UK
SOURCE: Brit. UK Pat. Appl., 18 pp.
CODEN: BAXXDU
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2065121	A	19810624	GB 1980-39322	19801208 <--
PRIORITY APPLN. INFO.:			GB 1979-43041 A	19791213
OTHER SOURCE(S):	CASREACT 96:19985			

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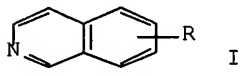


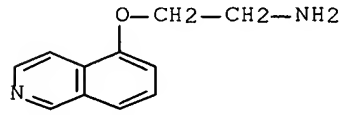
I

AB Isoquinoline derivs. I [R = 5-, 6-, 7-, 8-CH2OC6H4R1 [R1 = CO2R2 (R2 = H, C1-4 alkyl), CONHR3 (R3 = H, C1-4 alkyl, C2-4 alkanoyl, aroyl, C1-4 alkylsulfonyl, arylsulfonyl, aryl, aralkyl, 5- or 6-membered aromatic heterocyclyl optionally substituted by 1 or 2 C1-4 alkyl, C1-4 alkoxy, halo, CF3), CONR42 (R4 = C1-4 alkyl, NR42 = pyrrolidino, piperidino), NHR5 (R5 = H, C1-4 alkyl, C2-4 alkanoyl, C1-4 alkylsulfonyl, C1-4 alkoxycarbonyl; NHCONHR6 (R6 = C1-4 alkyl, aryl), CN, 5-tetrazolyl, 5-oxo-2-pyrazolin-1-yl, 3-methyl-5-oxo-2-pyrazolin-1-yl]; R = 5-, 6-, 7-, 8-OZR1 [Z = (CH2)n (n = 1-4), C6H4, CH2C6H4, CH2Z1 (Z1 = C-linked 5- or 6-membered aromatic heterocyclylidene); R1 as before]] were prepared I selectively inhibit thromboxane synthetase without significantly inhibiting prostacyclin synthetase or cyclooxygenase. I are thus useful in the treatment of thrombosis, ischemic heart disease, stroke, transient ischemic attack, migraine, and the vascular complications of diabetes. E.g., I [R = 5-(CH2)2CN] was prepared by treating I (R = 5-OH) with CH2:CHCN in the presence of PhCH2N+Me3 OH- (EtOH, reflux, 16 h).

IT **80278-33-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylsulfonylation of)

RN 80278-33-7 HCAPLUS

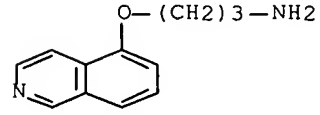
CN Ethanamine, 2-(5-isoquinolinyloxy)- (9CI) (CA INDEX NAME)



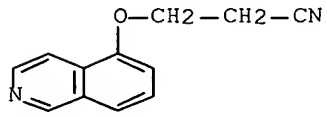
IT **80278-66-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and addition reaction of, with Me isocyanate)

RN 80278-66-6 HCAPLUS

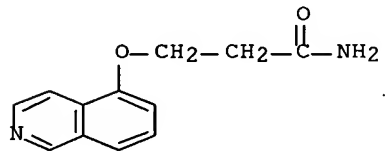
CN 1-Propanamine, 3-(5-isoquinolinyloxy)- (9CI) (CA INDEX NAME)



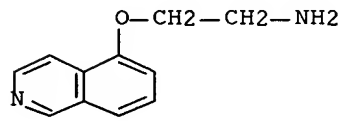
IT **80278-21-3P 80278-22-4P 80278-28-0P**
80278-29-1P 80278-33-7P 80278-37-1P
80278-38-2P 80278-40-6P 80278-59-7P
80289-36-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as thromboxane A2 synthetase **inhibitor**)
RN 80278-21-3 HCAPLUS
CN Propanenitrile, 3-(5-isoquinolinyloxy)- (9CI) (CA INDEX NAME)



RN 80278-22-4 HCAPLUS
CN Propanamide, 3-(5-isoquinolinyloxy)- (9CI) (CA INDEX NAME)

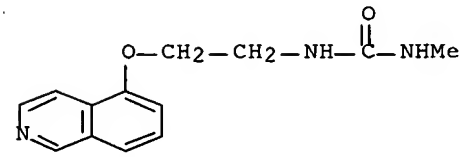


RN 80278-28-0 HCAPLUS
CN Ethanamine, 2-(5-isoquinolinyloxy)-, dihydrochloride (9CI) (CA INDEX NAME)

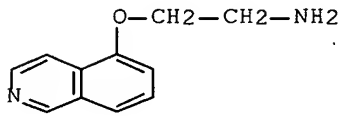


●2 HCl

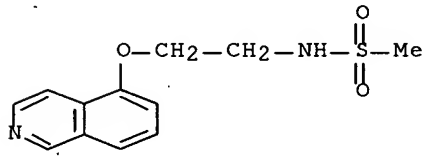
RN 80278-29-1 HCAPLUS
CN Urea, N-[2-(5-isoquinolinyloxy)ethyl]-N'-methyl- (9CI) (CA INDEX NAME)



RN 80278-33-7 HCAPLUS
CN Ethanamine, 2-(5-isoquinolinyloxy)- (9CI) (CA INDEX NAME)



RN 80278-37-1 HCAPLUS
CN Methanesulfonamide, N-[2-(5-isoquinolinyloxy)ethyl]- (9CI) (CA INDEX NAME)



RN 80278-38-2 HCAPLUS
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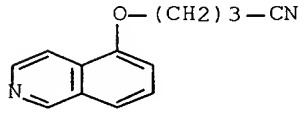
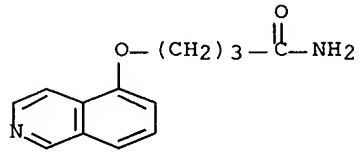
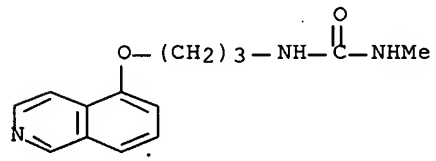


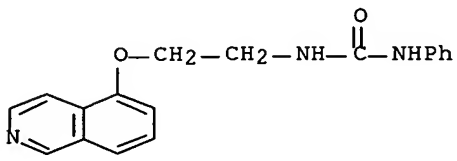
RN 80278-40-6 HCAPLUS
CN Butanamide, 4-(5-isoquinolinyloxy)- (9CI) (CA INDEX NAME)



RN 80278-59-7 HCAPLUS
CN Urea, N-[3-(5-isoquinolinyloxy)propyl]-N'-methyl- (9CI) (CA INDEX NAME)



RN 80289-36-7 HCAPLUS
CN Urea, N-[2-(5-isoquinolinyloxy)ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)



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